SEARCH REQUEST FORM

Requestor's Name: Jeffrey E Russel (1654) Serial Number: 09/674,526

Date: 3-24-2004 Phone: 571-272-0969 (wk) Art Unit: 1654

REM 3D19 (office) 3D11 (mailbox)

Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevent citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevent claim(s).

Please search the sequences SEQ ID NO:1 GGFG and SEQ ID NO 2 GGGF in STN. Please set the sequence length at SOL 4. If necessary, please use the keywords conjugat?, link?, carrier.

Thank you

JR

D.L. 3.25.04

STAFF USE ONLY

Point of Contact: Alexandra Waclawiw Technical Info. Specialist ~~CM1 6A02 Tel. 308-4491~~ 3-25-04

Date completed: _____

Searcher: Dom 1A71 2-2534

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CPU time: _____

Total time: _____

Number of Searches: _____

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_____ STIC

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_____ Pre-S

Type of Search

_____ N.A. Sequence

_____ A.A. Sequence

_____ Structure

Vendors

PVP 6

_____ IG 10

_____ STN 5

_____ Dialog

_____ APS 15

_____ Geninfo

_____ SDC

_____ DARC/Questel

Russel 09/674,526

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     FILE 'REGISTRY' ENTERED AT 08:28:54 ON 25 MAR 2004
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L1         49145 SEA FILE=REGISTRY ABB=ON  PLU=ON  GGFG|GGGF/SQSP
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L2           138 S L1 AND SQL=4

     FILE 'CAPLUS' ENTERED AT 08:30:01 ON 25 MAR 2004
L3            71 S L2
L4            32 S L3 AND (CONJUGAT? OR LINK? OR CARRIER?)
                 SELECT RN L4 1-32 HIT

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STRUCTURE FILE UPDATES:   24 MAR 2004  HIGHEST RN 667234-34-6
DICTIONARY FILE UPDATES:  24 MAR 2004  HIGHEST RN 667234-34-6

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

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=> d que l2
L1         49145 SEA FILE=REGISTRY ABB=ON  PLU=ON  GGFG|GGGF/SQSP
L2           138 SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 AND SQL=4

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SQ search 4 aa length

FILE COVERS 1907 - 25 Mar 2004 VOL 140 ISS 13
FILE LAST UPDATED: 24 Mar 2004 (20040324/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

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L3            71 SEA FILE=CAPLUS ABB=ON  PLU=ON  L2
L4            32 SEA FILE=CAPLUS ABB=ON  PLU=ON  L3 AND (CONJUGAT?/OBI OR
                 LINK?/OBI OR CARRIER?/OBI)
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L2           138 SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 AND SQL=4
L3            71 SEA FILE=CAPLUS ABB=ON  PLU=ON  L2
L4            32 SEA FILE=CAPLUS ABB=ON  PLU=ON  L3 AND (CONJUGAT?/OBI OR
                 LINK?/OBI OR CARRIER?/OBI)


=> d .ca l4 1-32

L4   ANSWER 1 OF 32  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2003:434299  CAPLUS
DOCUMENT NUMBER:          139:30773
TITLE:                    Peptides that bind to p185, and methods for the
                          treatment and diagnosis of tumors
INVENTOR(S):              Greene, Mark I.; Murali, Ramachandran; Berezov, Alan
PATENT ASSIGNEE(S):       The Trustees of the University of Pennsylvania, USA
SOURCE:                   PCT Int. Appl., 75 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND  DATE          APPLICATION NO.  DATE
     ----------------    ----  --------      ---------------  --------
     WO 2003045309        A2   20030605      WO 2002-US37390  20021121
     WO 2003045309        A3   20031218
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT,
             TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ,
             MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
     US 2003148932        A1   20030807      US 2002-301499   20021121
PRIORITY APPLN. INFO.:                     US 2001-331935P  P  20011121
OTHER SOURCE(S):          MARPAT 139:30773
AB   Peptides and pharmaceutical compns. comprising them are disclosed.
     Conjugated peptides linked to detectable agents and/or cytotoxic agents.
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are disclosed. A method of detecting tumors that have cell-surface p185 is disclosed. Methods of preventing transformation of a normal cell into a tumor cell in an individual at risk of developing a tumor having tumor cells which have p185 on their surfaces are disclosed. Methods of treating an individual who has cancer characterized by tumor cells that have a p185 on their cell surfaces are disclosed.

IC ICM A61K

CC 1-6 (Pharmacology)
Section cross-reference(s): 8, 14, 63

IT Cytotoxic agents
(and detectable agents, peptide **conjugates**; peptides binding to p185 for treatment and diagnosis of tumors)

IT Chelating agents
Linking agents
(chelating **linker**; peptides binding to p185 for treatment and diagnosis of tumors)

IT Toxins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**conjugates**, with peptides; peptides binding to p185 for treatment and diagnosis of tumors)

IT Peptides, biological studies
RL: DGN (Diagnostic use); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**conjugates**; peptides binding to p185 for treatment and diagnosis of tumors)

IT Radionuclides, biological studies
RL: DGN (Diagnostic use); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptide **conjugates**; peptides binding to p185 for treatment and diagnosis of tumors)

IT 67-43-6, DTPA 60239-18-1, DOTA
RL: RCT (Reactant); RACT (Reactant or reagent)
(chelating **linker**; peptides binding to p185 for treatment and diagnosis of tumors)

IT 14133-76-7, Technetium-99, biological studies
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(metastable, peptide **conjugates**; peptides binding to p185 for treatment and diagnosis of tumors)

IT 10098-91-6, Yttrium-90, biological studies 13981-56-1, Fluorine-18, biological studies
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(peptide **conjugates**; peptides binding to p185 for treatment and diagnosis of tumors)

IT 241813-38-7 359887-31-3 359887-32-4 359887-36-8 359887-38-0
359887-40-4 359887-42-6 359887-44-8 535959-77-4 535959-78-5
535959-79-6 535959-80-9 535959-81-0 535959-82-1 535959-83-2
535959-84-3 535959-85-4 535959-86-5 535959-87-6 535959-88-7
535959-89-8 535959-90-1 535959-91-2 535959-92-3 535959-93-4
535959-94-5 535959-95-6 535959-96-7 535959-99-0D, **conjugates**
with detectable or cytotoxic agents 535960-00-0D, **conjugates**
with detectable or cytotoxic agents 535960-01-1D, **conjugates**
with detectable or cytotoxic agents 535960-02-2D, **conjugates**
with detectable or cytotoxic agents 535960-03-3D, **conjugates**
with detectable or cytotoxic agents 535960-04-4D, **conjugates**
with detectable or cytotoxic agents 535960-05-5D, **conjugates**
with detectable or cytotoxic agents 535960-06-6D, **conjugates**
with detectable or cytotoxic agents
RL: DGN (Diagnostic use); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(peptides binding to p185 for treatment and diagnosis of tumors)

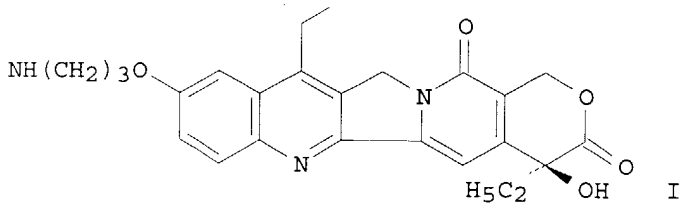
IT 5550-81-2 **75853-32-6** 403700-66-3 540490-74-2 540490-75-3
540490-76-4 540490-77-5 540490-78-6 540490-79-7 540490-80-0
540490-81-1 540490-82-2 540490-83-3 540490-84-4 540490-85-5
540490-86-6 540490-87-7 540490-88-8 540490-89-9 540490-90-2
540490-91-3 540490-92-4 540490-93-5 540490-94-6 540490-95-7
540490-96-8 540490-97-9 540490-98-0 540490-99-1 540491-00-7
540491-01-8 540491-02-9 540491-03-0 540491-04-1 540491-05-2
540491-06-3 540491-07-4 540491-08-5 540491-09-6 540491-10-9
540491-11-0 540491-12-1 540491-13-2 540491-14-3 540491-15-4
540491-16-5 540491-17-6 540491-18-7 540491-19-8 540491-20-1
540491-21-2 540491-22-3 540491-23-4 540491-24-5
RL: PRP (Properties)
(unclaimed sequence; peptides that bind to p185, and methods for the treatment and diagnosis of tumors)

L4 ANSWER 2 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:154283 CAPLUS
DOCUMENT NUMBER: 138:198591
TITLE: Polysaccharide-camptothecin derivative **conjugates** for inhibiting the metastasis or preventing the recurrence of malignant tumor
INVENTOR(S): Kawaguchi, Takayuki; Okuno, Satoshi; Yano, Toshiro
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003015826	A1	20030227	WO 2002-JP8309	20020816
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
JP 2003137818	A2	20030514	JP 2002-239094	20020820
US 2003092608	A1	20030515	US 2002-224475	20020821

PRIORITY APPLN. INFO.: JP 2001-249717 A 20010821
US 2001-331255P P 20011113

OTHER SOURCE(S): MARPAT 138:198591
GI



I

AB A pharmaceutical composition for inhibiting the metastasis or preventing the recurrence of a malignant tumor, which comprises as the active ingredient a polysaccharide derivative comprises a polysaccharide having a carboxyl group bound to an active substance having an antitumor activity via an amino acid or a peptide consisting of 2 to 8 amino acids which are the same or different, or a salt thereof. Preferred active substances are camptothecin derivs. I was prepared and exhibited excellent activity of prolonging lifetime in M5076 liver metastatic models.

IC ICM A61K047-48
ICS A61P035-04

CC 1-6 (Pharmacology)
Section cross-reference(s): 26, 33, 34

ST polysaccharide camptothecin deriv **conjugate** antitumor

IT Neoplasm
(metastasis; polysaccharide-camptothecin derivative **conjugates** for inhibiting the metastasis or preventing the recurrence of malignant tumor)

IT Antitumor agents
(polysaccharide-camptothecin derivative **conjugates** for inhibiting the metastasis or preventing the recurrence of malignant tumor)

IT 9004-54-0, Dextran, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(polyalc.; polysaccharide-camptothecin derivative **conjugates** for inhibiting the metastasis or preventing the recurrence of malignant tumor)

IT 187803-34-5DP, **conjugate** with carboxymethyl dextran
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(polysaccharide-camptothecin derivative **conjugates** for inhibiting the metastasis or preventing the recurrence of malignant tumor)

IT 9044-05-7D, Carboxymethyl dextran, **conjugate** with taxol and camptothecin derivs. 28320-73-2 39422-83-8, Carboxymethyl dextran sodium salt **187794-49-6** 288247-87-0 499982-21-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(polysaccharide-camptothecin derivative **conjugates** for inhibiting the metastasis or preventing the recurrence of malignant tumor)

IT 144008-87-7P 187794-70-3P 499982-17-1P 499982-19-3P **499982-23-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(polysaccharide-camptothecin derivative **conjugates** for inhibiting the metastasis or preventing the recurrence of malignant tumor)

IT **223537-08-4P 223537-10-8DP**, **conjugate** with polyalc. carboxymethyl dextran 499982-18-2DP, **conjugate** with carboxymethyl dextran 499982-20-6DP, **conjugate** with carboxymethyl dextran
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(polysaccharide-camptothecin derivative **conjugates** for inhibiting the metastasis or preventing the recurrence of malignant tumor)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:94089 CAPLUS
DOCUMENT NUMBER: 138:158804
TITLE: Optimized prodrugs as DDS for targeting to tumors
INVENTOR(S): Inoue, Kazuhiro; Kuga, Hiroshi; Kumasawa, Eiji; Shiose, Yoshinobu; Ousu, Satoru; Oki, Hitoshi
PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 20 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003034653	A2	20030207	JP 2001-250877	20010717

PRIORITY APPLN. INFO.: JP 2001-250877 20010717

AB The prodrugs comprising carriers, peptide spacers, and drugs, e.g. antitumor agents, analgesics, inflammation inhibitors, etc., show neither long-term in vivo accumulation nor immunogenicity, and are selectively accumulated in tumors based on EPR (enhanced permeability and retention) and released upon cleavage in the spacer part by peptidase. The prodrugs have significantly broadened therapeutic range and the carriers cleaved from the prodrugs have proper excretion property. The carriers are preferably derived from carboxymethyl dextran polyalc., which show improved flexibility of mol. chain, increased hydrophilicity, and stealth property, i.e. ability to escape recognition by macrophages. Conjugates of carboxymethyl dextran polyol with amide of (1S,9S)-1-amino-9-ethyl-5-fluoro-2,3-dihydro-9-hydroxy-4-methyl-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-10,13(9H,15H)-dione with Gly-Gly-Phe-Gly was prepared, and tissue distribution and antitumor effect of the prodrug were determined in mice.

IC ICM A61K045-00
ICS A61K031-4741; A61K031-704; A61K047-36; A61K047-48; A61P035-00
CC 63-6 (Pharmaceuticals)
ST carboxymethyl dextran polyol **carrier** tumor targeting DDS; tetrapeptide spacer optimization antitumor prodrug; doxorubicin prodrug carboxymethyl dextran polyol **carrier** peptide spacer
IT Drug delivery systems
(**carriers**; optimized DDS for targeting to tumors comprising **carriers** such as carboxymethyl dextran polyols, peptide spacers, and drug)
IT Analgesics
Anti-inflammatory agents
Antitumor agents
Drug delivery systems
(optimized DDS for targeting to tumors comprising **carriers** such as carboxymethyl dextran polyols, peptide spacers, and drug)
IT Drug delivery systems
(prodrugs; optimized DDS for targeting to tumors comprising **carriers** such as carboxymethyl dextran polyols, peptide spacers, and drug)
IT Neoplasm
(targeting of; optimized DDS for targeting to tumors comprising

carriers such as carboxymethyl dextran polyols, peptide spacers, and drug)

IT Inflammation
Pain
(treatment of; optimized DDS for targeting to tumors comprising **carriers** such as carboxymethyl dextran polyols, peptide spacers, and drug)

IT **200427-88-9DP**, reaction products with drugs and carboxymethyl dextran polyols
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(optimized DDS for targeting to tumors comprising **carriers** such as carboxymethyl dextran polyols, peptide spacers, and drug)

IT 4905-26-4D, reaction products with drugs and carboxymethyl dextran polyols 9044-05-7D, Carboxymethyl dextran, oxidative cleavage products, amides with doxorubicin tetrapeptide derivs. 9044-05-7D, Carboxymethyl dextran, reaction products with tetrapeptide derivs. of antitumor agents 23214-92-8, Doxorubicin 60254-83-3D, reaction products with drugs and carboxymethyl dextran polyols 61370-88-5D, reaction products with drugs and carboxymethyl dextran polyols 61430-18-0D, reaction products with drugs and carboxymethyl dextran polyols 81466-43-5D, reaction products with drugs and carboxymethyl dextran polyols 87743-02-0D, reaction products with drugs and carboxymethyl dextran polyols 105468-17-5D, reaction products with drugs and carboxymethyl dextran polyols 107889-44-1D, reaction products with drugs and carboxymethyl dextran polyols 145903-95-3D, reaction products with drugs and carboxymethyl dextran polyols 154485-92-4D, reaction products with drugs and carboxymethyl dextran polyols 154485-95-7D, reaction products with drugs and carboxymethyl dextran polyols 171335-80-1 203381-63-9D, reaction products with drugs and carboxymethyl dextran polyols **223537-10-8D**, reaction products with carboxymethyl dextran 289625-27-0D, reaction products with drugs and carboxymethyl dextran polyols 395070-80-1D, reaction products with drugs and carboxymethyl dextran polyols 402751-87-5D, reaction products with drugs and carboxymethyl dextran polyols 494834-91-2D, reaction products with drugs and carboxymethyl dextran polyols 494834-92-3D, reaction products with drugs and carboxymethyl dextran polyols 494834-93-4D, reaction products with drugs and carboxymethyl dextran polyols 494834-94-5D, reaction products with drugs and carboxymethyl dextran polyols 494834-95-6D, reaction products with drugs and carboxymethyl dextran polyols 494834-96-7D, reaction products with drugs and carboxymethyl dextran polyols 494834-97-8D, reaction products with drugs and carboxymethyl dextran polyols 494834-98-9D, reaction products with drugs and carboxymethyl dextran polyols 494834-99-0D, reaction products with drugs and carboxymethyl dextran polyols 494835-00-6D, reaction products with drugs and carboxymethyl dextran polyols 494835-01-7D, reaction products with drugs and carboxymethyl dextran polyols 494835-02-8D, reaction products with drugs and carboxymethyl dextran polyols 494835-03-9D, reaction products with drugs and carboxymethyl dextran polyols 494835-04-0D, reaction products with drugs and carboxymethyl dextran polyols 494835-05-1D, reaction products with drugs and carboxymethyl dextran polyols 494835-06-2D, reaction products with drugs and carboxymethyl dextran polyols 494835-07-3D, reaction products with drugs and carboxymethyl dextran polyols 494835-08-4D, reaction products with drugs and carboxymethyl dextran polyols 494835-09-5D, reaction products with drugs and carboxymethyl dextran polyols 494835-10-8D, reaction products with drugs and carboxymethyl dextran polyols 494835-11-9D, reaction products with drugs and carboxymethyl dextran polyols 494835-12-0D, reaction products with drugs and carboxymethyl dextran polyols 494835-13-1D,

reaction products with drugs and carboxymethyl dextran polyols 494835-14-2D, reaction products with drugs and carboxymethyl dextran polyols 494835-15-3D, reaction products with drugs and carboxymethyl dextran polyols 494835-16-4D, reaction products with drugs and carboxymethyl dextran polyols 494835-17-5D, reaction products with drugs and carboxymethyl dextran polyols 494835-18-6D, reaction products with drugs and carboxymethyl dextran polyols 494835-19-7D, reaction products with drugs and carboxymethyl dextran polyols 494835-20-0D, reaction products with drugs and carboxymethyl dextran polyols 494835-21-1D, reaction products with drugs and carboxymethyl dextran polyols 494835-22-2D, reaction products with drugs and carboxymethyl dextran polyols 494835-23-3D, reaction products with drugs and carboxymethyl dextran polyols 494835-24-4D, reaction products with drugs and carboxymethyl dextran polyols 494835-25-5D, reaction products with drugs and carboxymethyl dextran polyols 494835-26-6D, reaction products with drugs and carboxymethyl dextran polyols 494835-27-7D, reaction products with drugs and carboxymethyl dextran polyols 494835-28-8D, reaction products with drugs and carboxymethyl dextran polyols 494835-29-9D, reaction products with drugs and carboxymethyl dextran polyols 494835-30-2D, amides with carboxymethyl dextran oxidative cleavage products
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(optimized DDS for targeting to tumors comprising **carriers** such as carboxymethyl dextran polyols, peptide spacers, and drug)

IT 20234-78-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reaction products with antitumor agents and carboxymethyl dextran polyols and; optimized DDS for targeting to tumors comprising **carriers** such as carboxymethyl dextran polyols, peptide spacers, and drug)

IT 9031-96-3, Peptidase
RL: CAT (Catalyst use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(spacer cleavage by; optimized DDS for targeting to tumors comprising **carriers** such as carboxymethyl dextran polyols, peptide spacers, and drug)

L4 ANSWER 4 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:849477 CAPLUS
DOCUMENT NUMBER: 137:348514
TITLE: High throughput screening methods using magnetic resonance imaging agents
INVENTOR(S): Meade, Thomas J.
PATENT ASSIGNEE(S): Metaprobe, Inc., USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002087632	A1	20021107	WO 2002-US14194	20020502

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002197648 A1 20021226 US 2002-139145 20020502

PRIORITY APPLN. INFO.: US 2001-288963P P 20010502

AB The invention relates to a wide variety of different methods and compns. that find use in high throughput screening applications utilizing magnetic resonance imaging (MRI) contrast agents. The invention provides a library of MRI contrast agents comprising a chelate, a paramagnetic metal ion, and a different candidate agent. The candidate agent may be covalently attached to the chelate, or indirectly attached to the chelate via a linker. Suitable candidate agents include peptides, carbohydrates, nucleic acids and lipids. The methods may be applicable for screening for protease-activated MRI contrast agents, for screening of animals pretreated with a drug candidate, for screening of transgenic animals, for imaging gene expression, for imaging disease progression, etc.

IC ICM A61K051-00
ICS A61M036-14

CC 8-1 (Radiation Biochemistry)
Section cross-reference(s): 1, 9, 14, 63

IT Carbohydrates, biological studies
Lipids, biological studies
Nucleic acids
Peptides, biological studies
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(gadolinium-complexed **conjugates**; high throughput screening methods using magnetic resonance imaging agents)

IT **Linking** agents
Photolysis
(high throughput screening methods using magnetic resonance imaging agents with photocleavable **linkers**)

IT 57-22-7D, Vincristine, gadolinium-complexed **conjugates**
865-21-4D, Vinblastine, gadolinium-complexed **conjugates**
7440-54-2D, Gadolinium, **conjugated** complexes 23214-92-8D, Doxorubicin, gadolinium-complexed **conjugates** 29767-20-2D, Vm-26, gadolinium-complexed **conjugates** 33069-62-4D, Paclitaxel, gadolinium-complexed **conjugates** 33419-42-0D, Etoposide, gadolinium-complexed **conjugates** 53643-48-4D, Vindesine, gadolinium-complexed **conjugates** 60239-18-1D, DOTA, gadolinium-complexed **conjugates** 83678-67-5D, Gadolinium-DOTA, **conjugates** 97682-44-5D, Irinotecan, gadolinium-complexed **conjugates** 114977-28-5D, Docetaxel, gadolinium-complexed **conjugates** 123948-87-8D, Topotecan, gadolinium-complexed **conjugates** 474958-03-7 474958-04-8 474958-05-9 474958-06-0 474958-08-2
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(high throughput screening methods using magnetic resonance imaging agents)

IT **75853-32-6** 211918-90-0 409334-94-7 409334-95-8 409334-97-0 474949-49-0 474949-51-4 474949-60-5 474949-64-9 474949-67-2 474949-72-9 474949-75-2
RL: PRP (Properties)
(unclaimed sequence; high throughput screening methods using magnetic resonance imaging agents)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:843946 CAPLUS
DOCUMENT NUMBER: 138:112124

TITLE: Characteristics of change in molecular weight of DE-310 which is a polymeric drug with storage time
AUTHOR(S): Takeuchi, Masahito; Asai, Masahide; Tomitsuka, Toshiaki; Sakai, Hideki; Abe, Masahiko
CORPORATE SOURCE: Tokyo Pharm. Res. Cent., Daiichi Pharm. Co., Ltd., Tokyo, 134-8630, Japan
SOURCE: Material Technology (Tokyo, Japan) (2002), 20(5), 242-247
CODEN: MTECFQ
PUBLISHER: Zairyo Gijutsu Kenkyu Kyokai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB Carboxymethyldextran polyalc. camptothecin conjugate, which is a novel polymeric drug, was synthesized, and is being developed as a code of DE-310. We studied on the effects of storage temperature, excipients, and water content on the change in weight-average mol. weight, Mw, of lyophilized samples containing DE-310. Mw of DE-310 in lyophilized samples with excipients increased with storage time, and relationship between the rate of the increment in Mw and storage temperature was able to be expressed as Arrhenius plot. In addition, the sample having high glass transition temperature, Tg, showed low degree of the increment in Mw. The lyophilized samples with disaccharides were higher Tg than one of samples with monosaccharides or sugar alcs. The lyophilized sample with maltose showed the highest Tg in the samples studied, and it was found that maltose especially suppressed increasing in Mw with storage time.

CC 63-5 (Pharmaceuticals)

IT 9044-05-7D, Carboxymethyldextran, polyalc. **conjugate** with camptothecin
RL: BCP (Biochemical process); PRP (Properties); BIOL (Biological study); PROC (Process)
(characteristics of change in mol. weight of DE-310 during storage)

IT **200427-88-9**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(spacer; characteristics of change in mol. weight of DE-310 during storage)

L4 ANSWER 6 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:148739 CAPLUS
DOCUMENT NUMBER: 136:205403
TITLE: DDS compounds of drugs having hydroxy groups
INVENTOR(S): Ousu, Satoru; Oki, Hitoshi; Naito, Hiroyuki; Hirotani, Kenji
PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 24 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002060351	A2	20020226	JP 2001-80188	20010321

PRIORITY APPLN. INFO.: JP 2000-79655 A 20000322
OTHER SOURCE(S): MARPAT 136:205403

AB The DDS (drug delivery system) compds. are represented by the formula AWN(R1)C(R2)(R3)OQ or PZN(R1)C(R2)(R3)OQ [A = polymeric carrier for drugs;

W = spacer containing amino acid or oligopeptide residue linked to N at the C-terminal; P = protective group for H or NH2; Z = amino acid residue or oligopeptide residue linked to N at the C-terminal; R1-R3 = H, (substituted) alkyl, (substituted) aryl, carboxyl, alkoxycarbonyl; 2 of R1-R3 may form 4- to 8-membered ring; OQ = residue of OH-containing drugs]. Tert-Bu 13-[[1-[2-amino-6-[4-[(E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]-7-benzyl-2,5,8,11-tetraoxo-3,6,9,12-tetraazatri-1-decylcarbamate (preparation given) showed 89% release of 1-[2-amino-6-[4-[(E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinol (I) in murine fibrosarcoma Meth-A cell homogenate at 40° and pH 4.5 and <1% release of I in a buffer at pH 4.5. I.v. administration of a carboxymethyl dextran polyol derivative of I (linked through an oligopeptide and aminomethylene linker) at 10 mg/kg as I showed significant antitumor effect and did not cause diarrhea in mice.

IC ICM A61K047-48
ICS A61K031-506; A61K047-36; A61K047-42; A61P029-00; A61P035-00; C07K005-103

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 33, 34

ST DDS peptide polysaccharide **carrier** antitumor drug; dextran **carrier** peptide spacer antitumor DDS

IT Polysaccharides, biological studies
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug **carriers**; preparation of amino acid or peptide derivs. of hydroxy-containing drugs for DDS)

IT 39422-83-8DP, Carboxymethyldextran sodium salt, polyols, **conjugates** with peptide spacers and antitumor drugs
401470-32-4P 401470-34-6DP, **conjugates** with carboxymethyl dextran polyols **401470-36-8DP**, **conjugates** with carboxymethyl dextran polyols 401470-38-0DP, **conjugates** with carboxymethyl dextran polyols 401470-40-4DP, **conjugates** with carboxymethyl dextran polyols 401470-44-8DP, **conjugates** with carboxymethyl dextran polyols 401470-48-2DP, **conjugates** with carboxymethyl dextran polyols 401470-52-8DP, **conjugates** with carboxymethyl dextran polyols 401470-56-2DP, **conjugates** with carboxymethyl dextran polyols
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid or peptide derivs. of hydroxy-containing drugs for DDS)

IT 60667-52-9P 401470-30-2P 401470-31-3P 401470-33-5P 401470-34-6P **401470-35-7P** **401470-36-8P** 401470-37-9P 401470-38-0P 401470-39-1P 401470-40-4P 401470-41-5P 401470-42-6P 401470-43-7P 401470-44-8P 401470-45-9P 401470-46-0P 401470-47-1P 401470-48-2P 401470-49-3P 401470-50-6P 401470-51-7P 401470-52-8P 401470-53-9P 401470-54-0P 401470-55-1P 401470-56-2P 401470-58-4P 401470-60-8P 401470-61-9P 401470-62-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of amino acid or peptide derivs. of hydroxy-containing drugs for DDS)

L4 ANSWER 7 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:77429 CAPLUS
DOCUMENT NUMBER: 136:139833
TITLE: Drug **conjugates** containing dicarboxy C1-3

alkyldextran polyalcohols
INVENTOR(S): Inoue, Kazuhiro; Suzaki, Hiroshi
PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002030002	A2	20020129	JP 2000-215919	20000717

PRIORITY APPLN. INFO.: JP 2000-215919 20000717

AB The invention relates to a drug conjugate wherein a dicarboxy C1-3 alkyldextran polyalc. is bonded to the residue of a medicinal compound, e.g. an antitumor agent and an antiinflammatory agent, with/without of a spacer consisting of one amino acid or a spacer consisting of 2-8 amino acids bonded to each other via peptide bonds. The conjugate exhibits excellent drug targeting property. Dextran polyalc. was reacted with diethylbromomalonate in the presence of cesium hydroxide to obtain dicarboxymethyl dextran polyalc. sodium salt. Cisplatin was reacted with AgNO3 and then, with the obtained dicarboxymethyl dextran polyalc. sodium salt. to make a conjugate. The conjugate showed sustained-release of low-mol.weight Pt compound in phosphate buffer.

IC ICM A61K047-48
ICS A61K031-282; A61K031-337; A61K031-4745; A61K031-505; A61K033-24; A61K045-00; A61P029-00; A61P035-00; C08B037-02

CC 63-6 (Pharmaceuticals)

ST dicarboxyalkyl dextran polyalc drug **conjugate** prepn targeting

IT Anthracyclines
Taxanes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor agents; drug **conjugates** containing dicarboxy C1-3 alkyldextran polyalcs.)

IT Carboxylic acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(dicarboxylic, C1--3 alkyl, halogenated; preparation of drug **conjugates** containing dicarboxy C1-3 alkyldextran polyalcs.)

IT Anti-inflammatory agents
Antitumor agents
Drug delivery systems
(drug **conjugates** containing dicarboxy C1-3 alkyldextran polyalcs.)

IT Amino acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug **conjugates** containing dicarboxy C1-3 alkyldextran polyalcs. and amino acid spacers)

IT Peptides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug **conjugates** containing dicarboxy C1-3 alkyldextran polyalcs. and peptide spacers)

IT Alkaloids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vinca, antitumor agents; drug **conjugates** containing dicarboxy C1-3 alkyldextran polyalcs.)

IT 59-30-3, Folic acid, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; drug **conjugates** containing dicarboxy C1-3 alkyldextran polyalcs.)

IT 289-95-2D, Pyrimidine, fluoro derivs., **conjugates** with dicarboxyalkyl dextran polyalcs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor agents; drug **conjugates** containing dicarboxy C1-3 alkyldextran polyalcs.)

IT 9004-54-0DP, Dextran, polyalcs., dicarboxymethyl derivs., **conjugates** with antitumor agents or antiinflammatory agents with/without of peptide spacers, biological studies
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug **conjugates** containing dicarboxy C1-3 alkyldextran polyalcs.)

IT 7689-03-4D, Camptothecin, derivs., **conjugates** with dicarboxyalkyl dextran polyalcs. 41575-94-4D, Carboplatin, **conjugates** with dicarboxyalkyl dextran polyalcs. 61825-94-3D, Oxaliplatin, **conjugates** with dicarboxyalkyl dextran polyalcs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug **conjugates** containing dicarboxy C1-3 alkyldextran polyalcs.)

IT 685-87-0, Diethylbromomalonate 9004-54-0, Dextran T500, reactions 15663-27-1, Cisplatin 84275-35-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of drug **conjugates** containing dicarboxy C1-3 alkyldextran polyalcs.)

IT 41575-87-5P 60732-70-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of drug **conjugates** containing dicarboxy C1-3 alkyldextran polyalcs.)

IT 21351-79-1, Cesium hydroxide
RL: RGT (Reagent); RACT (Reactant or reagent)
(preparation of drug **conjugates** containing dicarboxy C1-3 alkyldextran polyalcs.)

IT 41575-87-5DP, **conjugates** with dicarboxymethyl dextran polyalcs. 60732-70-9DP, **conjugates** with dicarboxymethyldextranpolyalc.
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of drug **conjugates** containing dicarboxy C1-3 alkyldextran polyalcs.)

IT **200427-88-9DP**, **conjugates** with dicarboxymethyl dextran polyalcs. and antitumor or antiinflammatory drugs
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of drug **conjugates** containing dicarboxy C1-3 alkyldextran polyalcs. and peptide spacers)

L4 ANSWER 8 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:71911 CAPLUS
DOCUMENT NUMBER: 136:123681
TITLE: Pharmaceutical compositions containing DDS compounds
INVENTOR(S): Takahashi, Masayuki; Sugie, Shuichi; Takeuchi, Masahito
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002005855	A1	20020124	WO 2001-JP6020	20010711
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001071037	A5	20020130	AU 2001-71037	20010711
EP 1308171	A1	20030507	EP 2001-949945	20010711
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001012417	A	20030701	BR 2001-12417	20010711
NO 2003000139	A	20030313	NO 2003-139	20030110
US 2003148931	A1	20030807	US 2003-332706	20030113

PRIORITY APPLN. INFO.: JP 2000-213083 A 20000713
WO 2001-JP6020 W 20010711

AB Disclosed are pharmaceutical compns. which contain compds. obtained by bonding a carboxyl-bearing polysaccharide derivative to a camptothecin derivative either through a spacer or not there through and are improved in storage stability by the addition of a sugar or a sugar alc. and, if necessary, a pH regulator. (1S,9S)-1-amino-9-ethyl-5-fluoro-2,3-dihydro-9-hydroxy-4-methyl-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-10,13(9H,15H)-dione conjugates with carboxymethyldextran using Gly-Gly-Phe-Gly spacer, are formulated with maltose and pH modifier to pH 6-9 to have a freeze-dried composition

IC ICM A61K047-48
ICS A61K047-36; A61K047-26; A61K047-10; A61K009-19; A61K031-4745; C07D491-22

CC 63-6 (Pharmaceuticals)

ST camptothecin dextran **conjugate** freeze dried compn

IT Antitumor agents
(antitumor compns. containing camptothecin derivative **conjugates**)

IT Polysaccharides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor compns. containing camptothecin derivative **conjugates**)

IT Drug delivery systems
(freeze-dried; antitumor compns. containing camptothecin derivative **conjugates**)

IT Alcohols, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyhydric; antitumor compns. containing camptothecin derivative **conjugates**)

IT 50-69-1, Ribose 50-99-7, Glucose, biological studies 57-50-1, Saccharose, biological studies 58-86-6, Xylose, biological studies 59-23-4, Galactose, biological studies 63-42-3, Lactose 69-65-8, Mannitol 69-79-4, Maltose 87-89-8, Inositol 99-20-7, Trehalose 512-69-6, Raffinose 528-50-7, Cellobiose 1109-28-0, Maltotriose 3458-28-4, Mannose 9044-05-7D, Carboxymethyldextran, camptothecin derivative **conjugates** 171335-80-1D, **conjugates** with peptide and carboxymethyldextran **200427-88-9D**, **conjugates** with camptothecin derivative and carboxymethyldextran
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor compns. containing camptothecin derivative **conjugates**)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:10548 CAPLUS
DOCUMENT NUMBER: 136:74660
TITLE: DDS compounds containing drug-carboxymethyldextran polyalcohol **conjugates** and process for preparation thereof
INVENTOR(S): Imura, Akihiro; Noguchi, Shigeru; Yamaguchi, Tatsuya; Yagi, Tsutomu; Kawabe, Takefumi
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000734	A1	20020103	WO 2001-JP5498	20010627
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001067831	A5	20020108	AU 2001-67831	20010627
EP 1298145	A1	20030402	EP 2001-945629	20010627
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001012287	A	20030506	BR 2001-12287	20010627
NO 2002006212	A	20030206	NO 2002-6212	20021223
US 2003166513	A1	20030904	US 2003-297584	20030502

PRIORITY APPLN. INFO.: JP 2000-195919 A 20000629
WO 2001-JP5498 W 20010627

AB Disclosed is a DDS compound which comprises (1S,9S)-1-amino-9-Et-5-fluoro-2,3-dihydro-9-hydroxy-4-methyl-1H,12H-benzo[de]-pyrano[3',4':6,7]indolizino[1,2-b]quinoline-10,13(9H,15H)-dione (I) as the drug compound and carboxymethyldextran polyalc. and in which the 1-position amino group of the former is bonded to the carboxyl groups of the latter through a spacer consisting of either one amino acid or 2 to 8 amino acids bonded by peptide linkages, characterized in that the amount of the drug compound residue introduced is 3.2-8.4 % and that the carboxymethyldextran polyalc. has an average mol. weight of 240,000-480,000 and a degree of carboxymethylation of 0.14-0.47. Also disclosed is a process for the preparation of the DDS compound which comprises the step of adding an aqueous solution of sodium periodate to an aqueous solution of dextran at a temperature of 4° ± 2° to oxidize the dextran, and then adding the resulting reaction fluid to an aqueous solution of sodium borohydride at a temperature of ≤ 15° to thereby obtain dextran polyalc. A conjugate of I and carboxymethyldextran polyalc. with tetrapeptide spacer Gly-Gly-Phe-Gly was prepared, and its antitumor effect in Meth A cell-bearing mice was examined

IC ICM C08B037-02
ICS C07D491-22; A61K047-48; A61K031-4745; A61K047-36; A61P035-00

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
ST antitumor carboxymethyldextran polyalc **conjugate** peptide prepn
IT Antitumor agents
Drug delivery systems
Drug delivery systems
(preparation of antitumor drug-carboxymethyldextran polyalc. **conjugates** with peptide spacers)
IT 1892-57-5, 1-Ethyl-3-(dimethylaminopropyl)carbodiimide 25952-53-8
RL: RGT (Reagent); RACT (Reactant or reagent)
(condensation agents; preparation of antitumor drug-carboxymethyldextran polyalc. **conjugates** with peptide spacers)
IT 9044-05-7DP, Carboxymethyldextran, polyalcs., Na salts, **conjugates** with antitumor drug with peptide spacers 171335-80-1DP, **conjugates** with peptide spacers and carboxymethyldextran polyalcs. **384828-78-8DP**, reaction products with carboxymethyldextran polyalc.
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of antitumor drug-carboxymethyldextran polyalc. **conjugates** with peptide spacers)
IT 3926-62-3, Sodium monochloroacetate 9004-54-0, Dextran T-500, reactions 169869-90-3 **187794-49-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of antitumor drug-carboxymethyldextran polyalc. **conjugates** with peptide spacers)
IT 9004-54-0DP, Dextran, polyalcs. 9044-05-7DP, Carboxymethyldextran, polyalcs., Na salts **223537-08-4P 384828-78-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of antitumor drug-carboxymethyldextran polyalc. **conjugates** with peptide spacers)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:322648 CAPLUS
DOCUMENT NUMBER: 135:185307
TITLE: Characteristics of tissue distribution of various polysaccharides as drug **carriers**: influences of molecular weight and anionic charge on tumor targeting
AUTHOR(S): Sugahara, Shuichi; Okuno, Satoshi; Yano, Toshiro; Hamana, Hiroshi; Inoue, Kazuhiro
CORPORATE SOURCE: Drug Delivery System Institute, Ltd., Chiba, 278-0022, Japan
SOURCE: Biological & Pharmaceutical Bulletin (2001), 24(5), 535-543
CODEN: BPBLEO; ISSN: 0918-6158
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Using the Walker 256 model for carcinosarcoma-bearing rats, we i.v. administered 5 polysaccharide carriers with various mol. wts. (MWs) and elec. charges and tested for their plasma and tissue distribution. Two carriers, carboxymethylated-D-manno-D-glucan (CMMG) and CMdextran (CMDex), showed higher plasma AUC than the other carriers tested, namely, CMchitin (CMCh), N-desulfated N-acetylated heparin (DSH), and hyaluronic acid (HA). This was consistently found to be true over the range of MWs tested. For

CMDex, the maximum value of plasma AUC was obtained when the MW exceeded 150 kDa. As for the anionic charge, CMDex (110-180 kDa) with a degree of substitution (DS) of the CM groups ranging from 0.2 to 0.6, showed maximum plasma AUC values. Twenty-four hours after administration, the concentration of
CMDex (180-250 kDa; DS: 0.6-1.2) in tumors was more than 3% of dose/g-approx. 10-fold higher than those observed with CMCh, DSH and HA. Doxorubicin (DXR) was bound to these carriers via a peptide spacer, GlyGlyPheGly (GGFG), to give carrier-GGFG-DXR conjugates (DXR content: 4.2-7.0 (weight/weight)%), and the antitumor effects of these conjugates were tested with Walker 256 carcinosarcoma-bearing rats by monitoring the tumor wts. after a single i.v. injection. Compared with free DXR, CMDex-GGFG-DXR and CMMG-GGFG-DXR conjugates significantly suppressed tumor growth, while the CMCh-GGFG-DXR, DSH-GGFG-DXR, and HA-GGFG-DXR conjugates in a similar comparison showed weak tumor growth inhibition. These findings suggest that the antitumor effect of the carrier-DXR conjugates was related to the extent with which the carriers accumulated in the tumors.

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1, 33

ST doxorubicin polysaccharide **carrier** tumor targeting; antitumor doxorubicin **conjugate** polysaccharide charge mol wt

IT Polysaccharides, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(acidic, **conjugates** with doxorubicin and peptide; effects of mol. weight and anionic charge of polysaccharide drug **carriers** on tumor targeting)

IT Drug delivery systems
(**carriers**; effects of mol. weight and anionic charge of polysaccharide drug **carriers** on tumor targeting)

IT Polysaccharides, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(**conjugates**, with doxorubicin and peptide; effects of mol. weight and anionic charge of polysaccharide drug **carriers** on tumor targeting)

IT Polysaccharides, biological studies
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(effects of mol. weight and anionic charge of polysaccharide **carriers** on doxorubicin tissue distribution and tumor targeting)

IT Antitumor agents
Drug targeting
Molecular weight
(effects of mol. weight and anionic charge of polysaccharide drug **carriers** on tumor targeting)

IT 9067-32-7DP, Hyaluronic acid sodium salt, **conjugates** with doxorubicin and peptide 23214-92-8DP, Doxorubicin, **conjugates** with peptide and polysaccharides 39422-83-8DP, Carboxymethyl dextran sodium salt, **conjugates** with doxorubicin and peptide 65667-26-7DP, **conjugates** with doxorubicin and peptide 105156-94-3DP, Carboxymethyl chitin sodium salt, **conjugates** with doxorubicin and peptide **200427-88-9DP**, **conjugates** with

doxorubicin and polysaccharides 355129-33-8DP, **conjugates** with doxorubicin and peptide
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(effects of mol. weight and anionic charge of polysaccharide drug **carriers** on tumor targeting)

IT 9067-32-7P, Hyaluronic acid sodium salt 39422-83-8P, Carboxymethyl dextran sodium salt 65667-26-7P 105156-94-3P, Carboxymethyl chitin sodium salt 355129-33-8P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(effects of mol. weight and anionic charge of polysaccharide drug **carriers** on tumor targeting)

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:78410 CAPLUS
DOCUMENT NUMBER: 134:147856
TITLE: Preparation of polypeptide dendrimers as unimolecular **carriers** of diagnostic imaging contrast agents, bioactive substances and drugs
INVENTOR(S): Verdini, Antonio
PATENT ASSIGNEE(S): Italy
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001007469	A2	20010201	WO 2000-EP7022	20000721
WO 2001007469	A3	20010510		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1200461	A2	20020502	EP 2000-949393	20000721
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003506326	T2	20030218	JP 2001-512552	20000721
NZ 517231	A	20030530	NZ 2000-517231	20000721
NO 2002000333	A	20020122	NO 2002-333	20020122

PRIORITY APPLN. INFO.: IT 1999-FO15 A 19990723
WO 2000-EP7022 W 20000721

AB The invention describes new polypeptide dendrimers and processes for their synthesis. The polypeptide dendrimers of the invention have a structure which consists of a multifunctional core moiety from which highly branched polypeptide chains, formed by short peptide branching units, extend radially outwards. The outermost branches surround a lower d. space with

hollows and channels into which bioactive substances employed in diagnosis and therapy can be entrapped or covalently linked. The said polypeptide dendrimers are particularly useful in a number of areas in biol. and medicine as carriers for the delivery of bioactive substances, including drugs, or as carriers of bacterial, viral and parasite antigens, gene-therapy compds. and diagnostic imaging contrast agents. N[CH2CH2NHCOCH(CH2Ph)NH-Gly-Gly-Orn-Gly[Gly-Gly-Orn(Boc)-Gly-Boc]2]3 (Boc = tert-butoxycarbonyl) is an example of a polypeptide dendrimer which was synthesized. Various properties of the polypeptide dendrimers were studied, including stability to enzymic hydrolysis in vitro and immunogenicity in mice and its adjuvanticity when some of the NH2 groups are covalently linked to the octapeptide antigen Ala-Asn-Pro-Asn-Ala-Asn-Pro-Asn.

IC ICM C07K014-00

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 15, 63

ST peptide dendrimer prepn **carrier** drug imaging contrast agent; immunogen peptide dendrimer prepn

IT Imaging agents
(contrast; preparation of polypeptide dendrimers as unimol. **carriers** of diagnostic imaging contrast agents, bioactive substances and drugs)

IT Dendritic polymers
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptidyl; preparation of polypeptide dendrimers as unimol. **carriers** of diagnostic imaging contrast agents, bioactive substances and drugs)

IT Antibacterial agents
Antibiotics
Antitumor agents
Antiviral agents
Drug delivery systems
Gene therapy
(preparation of polypeptide dendrimers as unimol. **carriers** of diagnostic imaging contrast agents, bioactive substances and drugs)

IT Antigens
Peptides, preparation
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of polypeptide dendrimers as unimol. **carriers** of diagnostic imaging contrast agents, bioactive substances and drugs)

IT 322475-89-8DP, acetylated 322475-92-3DP, acetylated 322475-92-3P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(dendritic; preparation of polypeptide dendrimers as unimol. **carriers** of diagnostic imaging contrast agents, bioactive substances and drugs)

IT 322475-89-8P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dendritic; preparation of polypeptide dendrimers as unimol. **carriers** of diagnostic imaging contrast agents, bioactive substances and drugs)

IT 322641-30-5P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(initiator core for dendritic polypeptide; preparation of polypeptide dendrimers as unimol. **carriers** of diagnostic imaging contrast agents, bioactive substances and drugs)

IT 107-15-3P, 1,2-Ethanediamine, preparation 322641-29-2P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)
(initiator core for dendritic polypeptides; preparation of polypeptide dendrimers as unimol. **carriers** of diagnostic imaging contrast agents, bioactive substances and drugs)

IT 322475-87-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(initiator core for dendritic polypeptides; preparation of polypeptide dendrimers as unimol. **carriers** of diagnostic imaging contrast agents, bioactive substances and drugs)

IT **323178-52-5P**
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of polypeptide dendrimers as unimol. **carriers** of diagnostic imaging contrast agents, bioactive substances and drugs)

IT 105869-23-6DP, **conjugates** with polypeptide dendrimers
323178-48-9P 323178-51-4P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of polypeptide dendrimers as unimol. **carriers** of diagnostic imaging contrast agents, bioactive substances and drugs)

IT 556-50-3, Glycylglycine 2776-60-5, Glycylglycine methyl ester hydrochloride 4097-89-6, Tris(2-aminoethyl)amine 13734-34-4 139112-38-2, Tris(2-maleimidoethyl)amine 162827-98-7 322475-84-3 322475-90-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of polypeptide dendrimers as unimol. **carriers** of diagnostic imaging contrast agents, bioactive substances and drugs)

IT 322475-75-2P 322475-76-3P 322475-78-5P 322475-79-6P 322475-80-9P 322475-81-0P 322475-82-1P 322475-83-2P 322475-85-4P 322475-86-5P 322648-79-3P 322648-81-7P **323178-50-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of polypeptide dendrimers as unimol. **carriers** of diagnostic imaging contrast agents, bioactive substances and drugs)

L4 ANSWER 12 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:832857 CAPLUS
DOCUMENT NUMBER: 134:256691
TITLE: Determinants for the drug release from T-0128, camptothecin analog-carboxymethyl dextran **conjugate**
AUTHOR(S): Harada, M.; Sakakibara, H.; Yano, T.; Suzuki, T.; Okuno, S.
CORPORATE SOURCE: Discovery Research Laboratory, Tanabe Seiyaku Co. Ltd., Yodogawa-ku, Osaka, 532-8505, Japan
SOURCE: Journal of Controlled Release (2000), 69(3), 399-412
CODEN: JCREEC; ISSN: 0168-3659
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To improve pharmacol. profiles of camptothecins (CPTs), a new macromol. prodrug, denoted T-0128, was synthesized. This prodrug comprises a novel CPT analog (T-2513: 7-ethyl-10-aminopropyloxy-CPT) bound to carboxymethyl (CM) dextran through a Gly-Gly-Gly linker, with a mol. weight of 130 kDa. The present study was designed to elucidate the mechanisms that promote the release of linked T-2513. First, we compared the abilities of a rat liver homogenate, a cocktail of its lysosomal enzymes, and different types of pure enzymes, to liberate T-2513 from the conjugate. The releasing

rate in the homogenate was very slow, but was accelerated with the lysosomes. Lysosomal cysteine proteinases, such as cathepsin B, were responsible, coupled with the results of in vitro and in vivo inhibition studies using proteinase inhibitors. The pH optimum for the cathepsin B-mediated drug release was approx. 4. This corresponds to the pH in lysosomes, suggesting lysosomotropic release. Second, to assess the effect of the length and composition of the peptidyl linker, we synthesized the conjugates with a different linker and compared the drug-releasing rates. We found that the insertion of Phe into Gly-Gly-Gly allowed various kinds of enzymes to produce a rapid cleavage, and the Gly-chain lengthening enhanced the lysosome-mediated drug release. The released T-2513 levels in the liver and tumor of the tumor-bearing rats dosed with each conjugate increased with the length of Gly linker, suggesting a good in vitro to in vivo relationship. Comparative efficacy studies of the conjugates with a different linker demonstrated that T-0128 showed the maximum efficacy against MX-1 human mammary xenograft tumors. Thus the Gly-Gly-Gly linker exploits lysosomal cathepsin B to release T-2513 slowly and steadily, resulting in improved therapeutic efficacy.

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 26, 33, 34

ST camptothecin prodrug release dextran peptide **conjugate**

IT Antitumor agents
Dissolution rate
(determinants for drug release from T-0128 camptothecin analog-carboxymethyl dextran **conjugate**)

IT Drug delivery systems
(prodrugs; determinants for drug release from T-0128 camptothecin analog-carboxymethyl dextran **conjugate**)

IT 288247-87-0, T 2513
RL: PRP (Properties); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(determinants for drug release from T-0128 camptothecin analog-carboxymethyl dextran **conjugate**)

IT 187852-51-3P, Glycinamide, glycylglycylglycyl-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-, compound with dextran carboxymethyl ether sodium salt 187852-60-4P, Glycinamide, glycyl-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-, compound with dextran carboxymethyl ether sodium salt 187852-63-7P, T 0128 187852-64-8P, Glycinamide, glycylglycylglycylglycyl-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-, compound with dextran carboxymethyl ether sodium salt **193097-95-9P** 330808-09-8P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(determinants for drug release from T-0128 camptothecin analog-carboxymethyl dextran **conjugate**)

IT 4530-20-5, tert-Butoxycarbonylglycine 28320-73-2, Glycine, N-[(1,1-dimethylethoxy)carbonyl]glycylglycyl- 31972-52-8, tert-Butoxycarbonylglycylglycine 39422-83-8, Sodium carboxymethyl dextran 174308-47-5, Glycine, N-[(1,1-dimethylethoxy)carbonyl]glycylglycylglycyl- **187794-49-6** 330807-97-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(determinants for drug release from T-0128 camptothecin analog-carboxymethyl dextran **conjugate**)

IT **192991-32-5P 192991-33-6P** 330807-98-2P 330807-99-3P 330808-00-9P 330808-01-0P 330808-02-1P 330808-03-2P 330808-04-3P 330808-05-4P 330808-06-5P 330808-07-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(determinants for drug release from T-0128 camptothecin analog-carboxymethyl dextran **conjugate**)
IT 7689-03-4, Camptothecin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(determinants for drug release from T-0128 camptothecin analog-carboxymethyl dextran **conjugate**)
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:314580 CAPLUS
DOCUMENT NUMBER: 132:326152
TITLE: DDS compounds and method for assaying the same
INVENTOR(S): Susaki, Hiroshi; Inoue, Kazuhiro; Kuga, Hiroshi; Ikeda, Masahiro; Shiose, Yoshinobu; Korenaga, Hiroshi
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000025825	A1	20000511	WO 1999-JP6016	19991029
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9964880	A1	20000522	AU 1999-64880	19991029
AU 765409	B2	20030918		
BR 9915198	A	20010814	BR 1999-15198	19991029
EP 1155702	A1	20011121	EP 1999-952805	19991029
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2001002128	A	20010620	NO 2001-2128	20010430
ZA 2001004214	A	20020114	ZA 2001-4214	20010523

PRIORITY APPLN. INFO.: JP 1998-310130 A 19981030
JP 1998-329272 A 19981119
WO 1999-JP6016 W 19991029

AB The invention relates to a method for assaying a DDS compound containing a saccharide compound-modified carboxy C1-4 alkyldextran polyalc. and a drug compound [DX8951 or doxorubicin] residue bonded to this carboxy C1-4 alkyldextran polyalc., or a DDS compound wherein a polymer carrier is bonded to a drug compound residue via a spacer containing 2 to 8 amino acids bonded together via peptide bonds, which involves the step of assaying a hydrolyzate obtained by treating the DDS compound with peptidase.

IC ICM A61K047-48
ICS A61K047-30; A61K047-26; A61K031-47
CC 64-3 (Pharmaceutical Analysis)
Section cross-reference(s): 1, 63
IT 23214-92-8DP, Doxorubicin, **conjugates** with carboxy C1-4 alkyldextran polyalc. **carriers** 171335-80-1DP, DX 8951,

conjugates with carboxy C1-4 alkyldextran polyalc.
carriers
RL: ANT (Analyte); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(DDS compds. and method for assaying the same)

IT 9044-05-7DP, Carboxymethyldextran, polyalkyl and galactose- or N-acetylgalactosamine-modified, DX8951 or doxorubicin **conjugates** with **75853-32-6DP**, DX8951 or doxorubicin **conjugates** with carboxy C1-4 alkyldextran polyalc. and **200427-88-9DP**, DX8951 or doxorubicin **conjugates** with carboxy C1-4 alkyldextran polyalc. and 267227-43-0DP, DX8951 or doxorubicin **conjugates** with carboxy C1-4 alkyldextran polyalc. and
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(DDS compds. and method for assaying the same)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:311210 CAPLUS
DOCUMENT NUMBER: 133:155250
TITLE: Distribution characteristics of carboxymethyl pullulan-peptide-doxorubicin **conjugates** in tumor-bearing rats: different sequence of peptide spacers and doxorubicin contents
AUTHOR(S): Nogusa, Hideo; Yamamoto, Keiji; Yano, Toshiro; Kajiki, Masahiro; Hamana, Hiroshi; Okuno, Satoshi
CORPORATE SOURCE: Drug Delivery System Institute, Ltd., Chiba, 278-0022, Japan
SOURCE: Biological & Pharmaceutical Bulletin (2000), 23(5), 621-626
CODEN: BPBLEO; ISSN: 0918-6158
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Plasma and tissue distribution of conjugates of CM-pullulan (CMPul) and doxorubicin (DXR), either bound directly or through three types of tetrapeptide spacers, was studied after i.v. injection to rats bearing Walker 256 carcinosarcoma and compared with that of DXR. In contrast to DXR, each conjugate retained high levels of DXR in the conjugated form in plasma and displayed high accumulation in the tumor at 6 h after the administration. Disposition characteristics of [3H]CMPul in rats bearing Walker 256 carcinosarcoma indicate that pullulan, which had mol. weight over 50 kDa, is a suitable macromol. carrier for tumor targeting in cancer chemotherapy by carboxymethylation. We find that the in vivo antitumor effect of the conjugates depends on the tumor AUC of free DXR released from the conjugates. CMPul-DXR conjugates were also distributed in the reticuloendothelial organs, such as liver, spleen and bone marrow; however, the tissue concns. of the conjugates in the heart, lung and muscle were lower than those of DXR. We next investigated the effect of the DXR contents of CMPul-DXR conjugates on their body distribution in rats bearing Walker 256. The half life of CMPul-DXR conjugates in plasma were shorter and the conjugates had greater accumulation in the reticuloendothelial system, while they showed lower concns. in the tumor with increasing DXR contents. Antitumor activity of CMPul-DXR conjugates were reduced and the lethal toxicities of CMPul-DXR conjugates were amplified with increasing DXR contents.

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1

ST doxorubicin pullulan peptide **conjugate** pharmacokinetics antitumor

IT Structure-activity relationship
(antitumor; peptide spacers and doxorubicin contents effect on pharmacokinetics and antitumor activity of CM-pullulan-peptide-doxorubicin **conjugates** in tumor-bearing rats)

IT Drug delivery systems
(injections, i.v.; peptide spacers and doxorubicin contents effect on pharmacokinetics and antitumor activity of CM-pullulan-peptide-doxorubicin **conjugates** in tumor-bearing rats)

IT Antitumor agents
(peptide spacers and doxorubicin contents effect on pharmacokinetics and antitumor activity of CM-pullulan-peptide-doxorubicin **conjugates** in tumor-bearing rats)

IT 9057-02-7D, Pullulan, carboxymethyl derivs., reaction products with doxorubicin 23214-92-8D, Doxorubicin, reaction products with sodium carboxymethylpullulan **161254-06-4D**, reaction products with sodium carboxymethylpullulan 161254-07-5D, reaction products with sodium carboxymethylpullulan 161254-12-2D, reaction products with sodium carboxymethylpullulan
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(peptide spacers and doxorubicin contents effect on pharmacokinetics and antitumor activity of CM-pullulan-peptide-doxorubicin **conjugates** in tumor-bearing rats)

IT 23214-92-8, Doxorubicin
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(peptide spacers and doxorubicin contents effect on pharmacokinetics and antitumor activity of CM-pullulan-peptide-doxorubicin **conjugates** in tumor-bearing rats)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:146878 CAPLUS
DOCUMENT NUMBER: 132:288308
TITLE: Structure-activity relationships of carboxymethylpullulan-peptide-doxorubicin **conjugates**: Systematic modification of peptide spacers
AUTHOR(S): Nogusa, Hideo; Yano, Toshiro; Kashima, Nobukazu; Yamamoto, Keiji; Okuno, Satoshi; Hamana, Hiroshi
CORPORATE SOURCE: Drug Delivery System Institute, Ltd., Chiba, 278-0022, Japan
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(3), 227-230
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of carboxymethylpullulan (CMPul)-doxorubicin (DXR) conjugates bound by peptide spacers of different compns. and lengths were prepared and evaluated for their in vivo antitumor effects. Systematic study of the peptide spacers indicated that CMPul-DXR conjugates bound via appropriate dipeptide spacers were more potent than DXR.

CC 1-3 (Pharmacology)

Section cross-reference(s): 63
IT Structure-activity relationship
(antitumor; structure-antitumor activity relationships of CM-pullulan-peptide-doxorubicin **conjugates**)
IT Drug delivery systems
(prodrugs; structure-antitumor activity relationships of CM-pullulan-peptide-doxorubicin **conjugates**)
IT Antitumor agents
(structure-antitumor activity relationships of CM-pullulan-peptide-doxorubicin **conjugates**)
IT 23214-92-8D, Doxorubicin, **conjugates** with CM-pullulan and peptides 53571-87-2D, Carboxymethylpullulan, **conjugates** with peptidyl doxorubicin 264192-71-4D, **conjugates** with CM-pullulan **264192-72-5D**, **conjugates** with CM-pullulan 264192-73-6D, **conjugates** with CM-pullulan 264192-74-7D, **conjugates** with CM-pullulan 264192-75-8D, **conjugates** with CM-pullulan 264192-76-9D, **conjugates** with CM-pullulan 264192-77-0D, **conjugates** with CM-pullulan 264192-78-1D, **conjugates** with CM-pullulan 264192-79-2D, **conjugates** with CM-pullulan 264192-80-5D, **conjugates** with CM-pullulan 264192-81-6D, **conjugates** with CM-pullulan 264192-82-7D, **conjugates** with CM-pullulan 264192-83-8D, **conjugates** with CM-pullulan
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(structure-antitumor activity relationships of CM-pullulan-peptide-doxorubicin **conjugates**)
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:50615 CAPLUS
DOCUMENT NUMBER: 133:28087
TITLE: A triglycine **linker** improves tumor uptake and biodistributions of 67-Cu-Labeled anti-neuroblastoma MAb chCE7 F(ab')2 fragments
AUTHOR(S): Zimmermann, K.; Gianollini, S.; Schubiger, P. A.; Novak-Hofer, I.
CORPORATE SOURCE: Center for Radiopharmaceutical Sciences, Paul Scherrer Institute, Villigen, Switz.
SOURCE: Nuclear Medicine and Biology (1999), 26(8), 943-950
CODEN: NMBIEO; ISSN: 0969-8051
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The peptide-linked copper chelators CPTA-triglycyl-l-p-isothiocyanato-phenylalanine (CPTA-R1-NCS) as well as DOTA-triglycyl-l-p-isocyanato-phenylalanine (DOTA-R1-NCS) were synthesized and coupled to F(ab')2 fragments of the anti-neuroblastoma monoclonal antibody (MAb) chCE7. 67Cu-labeled conjugates were compared with the original CPTA- and DO3A-F(ab')2 in vitro and in vivo in mice bearing neuroblastoma xenografts. With the CPTA-R1-F(ab')2, biodistributions were improved, because radioactivity present in the kidney was reduced. With the DOTA-R1-F(ab')2, clearance from the blood was slower and tumor uptake was higher compared with the other conjugates. DOTA-R1-F(ab')2 achieved the best tumor/tissue ratios.
CC 8-9 (Radiation Biochemistry)
IT Drug delivery systems
(immunoconjugates, 67Cu-labeled; triglycine **linker** improves

tumor uptake and biodistributions of 67-Cu-Labeled anti-neuroblastoma MAb chCE7 F(ab')2 fragments)

IT Antibodies
RL: RCT (Reactant); RACT (Reactant or reagent)
(monoclonal, chCE7, F(ab')2 fragment; triglycine **linker** improves tumor uptake and biodistributions of 67-Cu-Labeled anti-neuroblastoma MAb chCE7 F(ab')2 fragments)

IT Antibodies
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monoclonal, labeled, 67Cu-labeled; triglycine **linker** improves tumor uptake and biodistributions of 67-Cu-Labeled anti-neuroblastoma MAb chCE7 F(ab')2 fragments)

IT Nerve, neoplasm
(neuroblastoma; triglycine **linker** improves tumor uptake and biodistributions of 67-Cu-Labeled anti-neuroblastoma MAb chCE7 F(ab')2 fragments)

IT Immunoradiotherapy
(triglycine **linker** improves tumor uptake and biodistributions of 67-Cu-Labeled anti-neuroblastoma MAb chCE7 F(ab')2 fragments)

IT **273944-80-2DP**, 67Cu-labeled MAb **conjugate**
273944-81-3DP, 67Cu-labeled MAb **conjugate**
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(triglycine **linker** improves tumor uptake and biodistributions of 67-Cu-Labeled anti-neuroblastoma MAb chCE7 F(ab')2 fragments)

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:763905 CAPLUS
DOCUMENT NUMBER: 132:15631
TITLE: Antitumor or antiinflammatory drug composites
INVENTOR(S): Susaki, Hiroshi; Inoue, Kazuhiro; Kuga, Hiroshi
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9961061	A1	19991202	WO 1999-JP2681	19990521
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2333321	AA	19991202	CA 1999-2333321	19990521
AU 9937333	A1	19991213	AU 1999-37333	19990521
EP 1080732	A1	20010307	EP 1999-919664	19990521
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
NO 2000005913	A	20010122	NO 2000-5913	20001122

PRIORITY APPLN. INFO.: JP 1998-140915 A 19980522
WO 1999-JP2681 W 19990521

AB Drug composites useful as DDS compds., which are represented by the general formula: A-R-NH-Y-CH2-O-CO-Q (wherein A is a polymer serving as a carrier for a drug; R is a spacer comprising one amino acid mol. or one comprising 2 to 8 amino acid mols. bound to each other through peptide linkage; Y is optionally substituted phenylene; and Q is a residue of a drug compound such as an antitumor agent). The composites permit the speedy and regioselective release of drug compds. such as antitumor or anti-inflammatory agents, thus exhibiting expected drug effects without fail. A composite of DX-8951 [(1S,9S)-1-Amino-9-ethyl-5-fluoro-2,3-dihydro-9-hydroxy-4-methyl-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-10,13(9H,15H)-dione] was prepared from DX-8951 methanesulfonic acid salt, dextran polyalc. Na salt, Boc-Gly-Gly-Phe-Gly-OH, 4-aminobenzylalc., and bis(4-nitrophenyl)carbonate.

IC ICM A61K047-48
ICS A61K047-36; A61K009-00; A61K031-47; C07D491-22

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

ST antitumor dextran polyalc peptide aminobenzyloxycarbonyl **conjugate** ; antiinflammatory dextran polyalc peptide aminobenzyloxycarbonyl **conjugate**

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aminobenzyloxycarbonyl, **conjugates** with antitumor or antiinflammatory drugs and carboxyalkyldextran polyalcs.; antitumor or antiinflammatory drug dextran polyalc. **conjugates**)

IT Anti-inflammatory agents
Antitumor agents
Drug bioavailability
Drug delivery systems
Drug targeting
(antitumor or antiinflammatory drug dextran polyalc. **conjugates**)

IT 64-19-7DP, Acetic acid, reaction products with dextran and Dx 8951 derivs., biological studies 9004-54-0DP, Dextran, polyalcs., **conjugates** with peptide-aminobenzyloxycarbonyl spacers and antitumor or antiinflammatory drugs, biological studies 9044-05-7DP, Carboxymethyldextran, polyalcs., **conjugates** with peptide-aminobenzyloxycarbonyl spacers and antitumor or antiinflammatory drugs 171335-80-1DP, DX 8951, reaction products with dextran-peptide-aminobenzyloxycarbonyl **conjugates** **251459-40-2DP**, reaction products with dextran and acetic acid 251459-41-3DP, reaction products with dextran and acetic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antitumor or antiinflammatory drug dextran polyalc. **conjugates**)

IT **251459-33-3DP**, reaction products with dextran and acetic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of antitumor or antiinflammatory drug dextran polyalc. **conjugates**)

IT 623-04-1, 4-Aminobenzylalcohol 5070-13-3, Bis(4-nitrophenyl)carbonate 169869-90-3 **187794-49-6** **251459-34-4**
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of antitumor or antiinflammatory drug dextran polyalc. **conjugates**)

IT 9044-05-7DP, Carboxymethyldextran, polyalcs., Na salts 31972-52-8P **251459-28-6P 251459-29-7P 251459-31-1P** **251459-32-2P** 251459-35-5P **251459-36-6P** 251459-37-7P **251459-38-8P** 251459-39-9P **251459-40-2DP**, reaction products with dextran and acetic acid 251459-41-3P **251459-42-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of antitumor or antiinflammatory drug dextran polyalc. **conjugates**)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:224542 CAPLUS
DOCUMENT NUMBER: 130:316621
TITLE: Drug **conjugates** comprising carboxyalkyl pullulan polyalcohol **carriers** bonded with pharmaceutically active agents through peptide spacers
INVENTOR(S): Inoue, Kazuhiro; Suzaki, Hiroshi; Ikeda, Masahiro
PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan; Dds Kenkyusho K. K.
SOURCE: Jpn. Kokai Tokkyo Koho, 12 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11092405	A2	19990406	JP 1997-254780	19970919

PRIORITY APPLN. INFO.: JP 1997-254780 19970919

AB The invention provides a drug conjugate suitable for an improved drug delivery system of an antitumor agent or an anti-inflammatory agent, wherein the conjugate contains a carboxy C1-4 alkyl pullulan polyalc. carrier bonded with a pharmaceutically active agent residue through a spacer consisting of an amino acid or a peptide with 2-8 amino acids. An antitumor conjugate consisting of carboxymethyl pullulan polyalc.-Gly-Gly-Phe-Gly-(DX-8951) was prepared The conjugate exhibited higher antitumor effect with lower injection doses in Meth A-bearing mice as compared with the effect of unconjugated DX-8951.

IC ICM A61K047-48
ICS C07K005-103
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 33
ST carboxyalkyl pullulan peptide spacer antitumor **conjugate**
IT Drug delivery systems
(**carriers**; drug **conjugates** comprising carboxyalkyl pullulan polyalc. **carriers** bonded with drugs through peptide spacers)
IT Anti-inflammatory agents
Antitumor agents
Drug delivery systems
Drug targeting
(drug **conjugates** comprising carboxyalkyl pullulan polyalc. **carriers** bonded with drugs through peptide spacers)
IT Drug delivery systems
(injections; drug **conjugates** comprising carboxyalkyl pullulan polyalc. **carriers** bonded with drugs through peptide spacers)

IT 79-11-8DP, reaction products with pullulan derivative and peptide-benzopyranoindolizinoquinoline **conjugate** 9057-02-7DP, Pullulan, oxidized, reduced, reaction products with chloroacetate and peptide-benzopyranoindolizinoquinoline **conjugate** 169869-90-3DP, reaction products with pullulan polyalc.-peptide **conjugate** 171335-80-1DP, reaction products with pullulan polyalc.-peptide **conjugate**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug **conjugates** comprising carboxyalkyl pullulan polyalc. **carriers** bonded with drugs through peptide spacers)

IT 23214-92-8D, Doxorubicin, reaction products with pullulan polyalc.-peptide **conjugate**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug **conjugates** comprising carboxyalkyl pullulan polyalc. **carriers** bonded with drugs through peptide spacers)

IT 79-11-8, reactions 9057-02-7, Pullulan **187794-49-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of drug **conjugates** comprising carboxyalkyl pullulan polyalc. **carriers** bonded with drugs through peptide spacers)

IT **223537-08-4P 223537-11-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of drug **conjugates** comprising carboxyalkyl pullulan polyalc. **carriers** bonded with drugs through peptide spacers)

L4 ANSWER 19 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:698781 CAPLUS
DOCUMENT NUMBER: 130:106984
TITLE: Comparison of 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid (DOTA)-peptide-ChL6, a novel immunoconjugate with catabolizable **linker**, to 2-iminothiolane-2-[p-(bromoacetamido)benzyl]-DOTA-ChL6 in breast cancer xenografts
AUTHOR(S): DeNardo, Gerald L.; Kroger, Linda A.; Meares, Claude F.; Richman, Carol M.; Salako, Qansy; Shen, Sui; Lamborn, Kathleen R.; Peterson, James J.; Miers, Laird A.; Zhong, Gao Ren; DeNardo, Sally J.
CORPORATE SOURCE: Department of Internal Medicine, School of Medicine, University of California Davis, Sacramento, CA, 95816, USA
SOURCE: Clinical Cancer Research (1998), 4(10), 2483-2490
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Radioimmunotherapy using 131I-ChL6 antibody has shown promise in patients with breast cancer. To enhance this potential, a novel ChL6 immunoconjugate that is catabolizable and tightly binds 90Y and 111In was developed. The immunoconjugate, 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid (DOTA)-peptide-ChL6, consists of the macrocyclic chelator DOTA linked to ChL6 by a peptide that is preferentially catabolized in the liver. The pharmacokinetic and dosimetric properties of the radioimmunoconjugates (RICs) 111In- and 90Y-DOTA-peptide-ChL6 and 111In- and 90Y-2-iminothiolane (2-IT)-2-[p-(bromoacetamido)benzyl]-DOTA-ChL6 were compared in athymic

mice bearing HBT3477 human breast cancer xenografts. Each of the RICs was stable in vivo and concentrated well in the xenografts. Liver concentration, cumulative radioactivity (activity over time), and radiation dose of the DOTA-peptide-ChL6 RICs were one-third to one-half of those of the corresponding 2-IT-2-[p(bromoacetamido)benzyl]-DOTA-ChL6 RICs. Indium-111 RICs were imperfect tracers for corresponding 90Y RICs, although their pharmacokinetics and radiation dosimetries were similar. The results of this study were consistent with previously published in vitro data, which indicated that the peptide linker of DOTA-peptide-ChL6 was catabolized by cathepsin B. The cumulative activities and radiation doses to the liver of DOTA-peptide-ChL6 RICs were one-half of those of corresponding RICs with the 2-IT linker. Preliminary data from pilot studies in patients with breast cancer are in accord with these observations. These novel DOTA-peptide RICs seem to have excellent clin. potential for radioimmunotherapy associated with marrow transplantation, for which liver radiation is likely to be dose limiting for 90Y.

CC 8-9 (Radiation Biochemistry)

IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**conjugates**; comparison of 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid (DOTA)-peptide-ChL6 radioimmunoconjugate to 2-iminothiolane-2-[p-(bromoacetamido)benzyl]-DOTA-ChL6 radioimmunoconjugate in breast cancer xenografts)

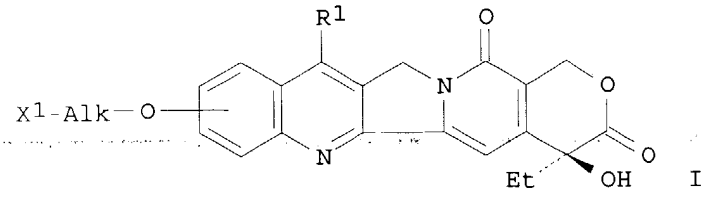
IT 6539-14-6D, 2-Iminothiolane, immunoconjugate with DOTA and ChL6 antibody **219721-93-4D**, radioimmunoconjugate with DOTA and ChL6 antibody
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparison of 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid (DOTA)-peptide-ChL6 to 2-iminothiolane-2-[p-(bromoacetamido)benzyl]-DOTA-ChL6 in breast cancer xenografts)

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

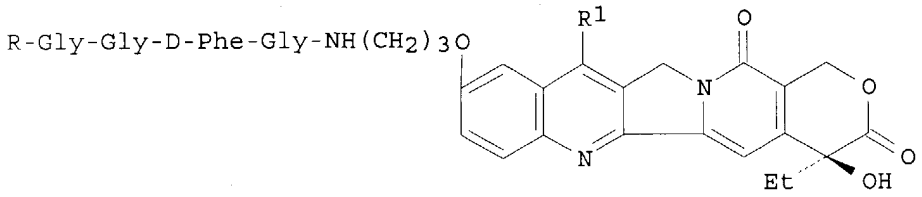
L4 ANSWER 20 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:665874 CAPLUS
DOCUMENT NUMBER: 130:4084
TITLE: Preparation of polysaccharide-peptide or amino acid-**linked** camptothecin **conjugates** as antitumor agents
INVENTOR(S): Tsujihara, Kenji; Kawaguchi, Takayuki; Okuno, Akira; Yano, Toshiaki
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 44 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10273488	A2	19981013	JP 1998-16763	19980129
JP 3322203	B2	20020909		

PRIORITY APPLN. INFO.: JP 1997-17280 A 19970131
OTHER SOURCE(S): MARPAT 130:4084
GI



I



II

AB The title compds., which are camptothecin derives. [I; R1 = (un)substituted lower alkyl; X1 = NHR2, OH; wherein R2 = H, lower alkyl; Alk = linear or branched alkylene optionally interrupted by O] linked to carboxy-containing polysaccharide through a peptide or amino acid, are prepared These compds. are reduced in toxicity and markedly enhanced in antitumor potency. Claimed is a pharmaceutical composition containing I as the active ingredient for treatment of cancers of lung, uterus, ovary, breast, digestive organs (large intestine, stomach, or pancreas), liver, kidney, prostate gland, and neck, malignant lymphoma, and leukemia. Thus, N-peptidyl-10-(3-aminopropoxy)-(20S)-camptothecin derivative (II; R = H) (preparation given) was condensed with carboxymethyl dextran sodium salt using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in H2O to give the title compound II (R = carboxymethyl dextran sodium salt residue), which at 60 mg/kg (single dosage) in vivo inhibited 100% the proliferation of human breast cancer MX-1 cell in mice within 26 days after the drug administration.

IC ICM C07D491-22
ICS A61K031-47

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

ST polysaccharide peptide **linked** camptothecin **conjugate** prepn; antitumor camptothecin **conjugate**; amino acid **linked** camptothecin polysaccharide prepn

IT Antitumor agents
Antitumor agents
(digestive tract; preparation of polysaccharide-peptide or amino acid-**linked** camptothecin **conjugates** as antitumor agents)

IT Liver, neoplasm
(hepatoma, inhibitors; preparation of polysaccharide-peptide or amino acid-**linked** camptothecin **conjugates** as antitumor agents)

IT Antitumor agents
(hepatoma; preparation of polysaccharide-peptide or amino acid-**linked** camptothecin **conjugates** as antitumor agents)

IT Kidney, neoplasm
Kidney, neoplasm

Lung, neoplasm
Pancreas, neoplasm
Pancreas, neoplasm
Stomach, neoplasm
Uterus, neoplasm
Uterus, neoplasm
(inhibitors; preparation of polysaccharide-peptide or amino acid-**linked** camptothecin **conjugates** as antitumor agents)

IT Antitumor agents
Antitumor agents
(kidney; preparation of polysaccharide-peptide or amino acid-**linked** camptothecin **conjugates** as antitumor agents)

IT Antitumor agents
(leukemia; preparation of polysaccharide-peptide or amino acid-**linked** camptothecin **conjugates** as antitumor agents)

IT Antitumor agents
(lung; preparation of polysaccharide-peptide or amino acid-**linked** camptothecin **conjugates** as antitumor agents)

IT Antitumor agents
(mammary gland; preparation of polysaccharide-peptide or amino acid-**linked** camptothecin **conjugates** as antitumor agents)

IT Antitumor agents
(neck; preparation of polysaccharide-peptide or amino acid-**linked** camptothecin **conjugates** as antitumor agents)

IT Digestive tract
Digestive tract
Mammary gland
Neck, anatomical
Neck, anatomical
Prostate gland
(neoplasm, inhibitors; preparation of polysaccharide-peptide or amino acid-**linked** camptothecin **conjugates** as antitumor agents)

IT Antitumor agents
Antitumor agents
(pancreas; preparation of polysaccharide-peptide or amino acid-**linked** camptothecin **conjugates** as antitumor agents)

IT Antitumor agents
(preparation of polysaccharide-peptide or amino acid-**linked** camptothecin **conjugates** as antitumor agents)

IT Amino acids, preparation
Glycoconjugates
Glycopeptides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of polysaccharide-peptide or amino acid-**linked** camptothecin **conjugates** as antitumor agents)

IT Antitumor agents
(prostate gland; preparation of polysaccharide-peptide or amino acid-**linked** camptothecin **conjugates** as antitumor agents)

IT Antitumor agents
(stomach; preparation of polysaccharide-peptide or amino acid-**linked** camptothecin **conjugates** as antitumor agents)

IT Antitumor agents
Antitumor agents
(uterus; preparation of polysaccharide-peptide or amino acid-**linked** camptothecin **conjugates** as antitumor agents)

IT 39422-83-8DP, Carboxymethyl dextran sodium salt, **conjugates** with peptide-**linked** camptothecin derivs. 53571-87-2DP, Carboxymethyl pullulan, **conjugates** with peptide-**linked**

camptothecin derivs., sodium salt 187793-65-3P 187793-71-1P
187794-13-4P 187794-21-4P 187794-24-7P 187794-27-0P 187794-30-5P
187794-33-8P 187794-36-1P **187803-18-5DP**, bound to
carboxymethyl dextran sodium salt 187803-20-9DP, bound to carboxymethyl
dextran sodium salt 187803-20-9DP, bound to carboxymethyl pullulan
sodium salt **187803-21-0DP**, bound to carboxymethyl dextran sodium
salt **187803-22-1DP**, bound to carboxymethyl dextran sodium salt
187803-23-2DP, bound to carboxymethyl dextran sodium salt
187803-26-5DP, bound to carboxymethyl dextran sodium salt
187803-27-6DP, bound to carboxymethyl dextran sodium salt
187803-28-7DP, bound to carboxymethyl dextran sodium salt
187803-29-8DP, bound to carboxymethyl dextran sodium salt
187803-30-1DP, bound to carboxymethyl dextran sodium salt
187803-31-2DP, bound to carboxymethyl dextran sodium salt 187803-32-3DP,
bound to carboxymethyl dextran sodium salt **187803-33-4DP**, bound
to carboxymethyl dextran sodium salt 187803-34-5DP, bound to
carboxymethyl dextran sodium salt 187803-35-6DP, bound to carboxymethyl
dextran sodium salt 215591-97-2DP, bound to carboxymethyl dextran sodium
salt 215591-98-3DP, bound to carboxymethyl dextran sodium salt
215592-03-3P 215592-06-6P 215592-09-9P 215592-15-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of polysaccharide-peptide or amino acid-**linked**
camptothecin **conjugates** as antitumor agents)

IT 79-11-8, Chloroacetic acid, reactions 98-59-9, Tosyl chloride
156-87-6, 3-Aminopropanol 627-30-5, 3-Chloropropanol 1826-67-1,
Vinylmagnesium bromide 3978-80-1 9004-54-0, Dextran, reactions
9057-02-7, Pullulan 15761-38-3 17302-47-5 18162-48-6,
tert-Butyldimethylsilyl chloride 24424-99-5, Di-tert-butyl dicarbonate
28782-81-2 42454-06-8, 5-Hydroxy-2-nitrobenzaldehyde 110351-94-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of polysaccharide-peptide or amino acid-**linked**
camptothecin **conjugates** as antitumor agents)

IT 39422-83-8P, Carboxymethyl dextran sodium salt 53571-87-2DP,
Carboxymethyl pullulan, sodium salt 58885-58-8P 80909-96-2P
187793-42-6P 187793-43-7P 187793-44-8P 187793-46-0P 187793-48-2P
187793-52-8P 187793-56-2P 187793-58-4P 187793-60-8P 187793-62-0P
187793-67-5P 187793-69-7P 187793-76-6P **187793-80-2P**
187793-82-4P 187793-84-6P 187793-86-8P
187794-01-0P 187794-03-2P 187794-05-4P 187794-07-6P 187794-09-8P
187794-11-2P 187794-17-8P 187794-19-0P 187794-20-3P 187794-22-5P
187794-23-6P 187794-25-8P 187794-26-9P 187794-28-1P 187794-29-2P
187794-31-6P 187794-32-7P 187794-34-9P 187794-35-0P 187794-47-4P
187794-50-9P 187794-55-4P 187794-58-7P
187794-60-1P 187794-66-7P 187794-68-9P 187794-70-3P
187794-72-5P **187794-74-7P** 187803-36-7P 187803-37-8P
205647-87-6P 215591-99-4P **215592-00-0P** 215592-01-1P
215592-02-2P 215592-04-4P 215592-05-5P 215592-07-7P 215592-08-8P
215592-10-2P 215592-11-3P 215592-12-4P **215592-13-5P**
215592-14-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of polysaccharide-peptide or amino acid-**linked**
camptothecin **conjugates** as antitumor agents)

L4 ANSWER 21 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:1393 CAPLUS
DOCUMENT NUMBER: 128:66510
TITLE: Process for producing drug complexes

Russel 09/674,526

INVENTOR(S): Inoue, Kazuhiro; Susaki, Hiroshi; Ikeda, Masahiro
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan; Inoue, Kazuhiro; Susaki, Hiroshi; Ikeda, Masahiro
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9746261	A1	19971211	WO 1997-JP1915	19970605
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
TW 409058	B	20001021	TW 1997-86107456	19970531
AU 9729788	A1	19980105	AU 1997-29788	19970605
AU 723442	B2	20000824		
CN 1227500	A	19990901	CN 1997-197115	19970605
EP 955064	A1	19991110	EP 1997-924326	19970605
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
NO 9805667	A	19990204	NO 1998-5667	19981204
KR 2000016371	A	20000325	KR 1998-709945	19981204
US 6291671	B1	20010918	US 1999-147341	19990322

PRIORITY APPLN. INFO.: JP 1996-144522 A 19960606
WO 1997-JP1915 W 19970605

AB The invention relates to a process for producing drug complexes wherein a carboxylated polysaccharide derivative is bonded to a medicinal compound residue via a spacer consisting of an amino acid or a spacer consisting of two to eight amino acids bonded to each other via peptide bonds, or drug complexes wherein a carboxylated polysaccharide derivative is bonded to a medicinal compound residue via no spacer, which is characterized by reacting in a nonaq. system an organic amine salt of the carboxylated polysaccharide derivative with the medicinal compound or the spacer bonded thereto. Thus, the reaction between the carboxylated polysaccharide derivative and the medicinal compound bonded to the spacer, etc., can be effected to achieve a high yield and side reactions can be inhibited in the case where, for example, the medicinal compound is one having a lactone ring.

IC ICM A61K047-48
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
ST anticancer antiinflammatory drug polysaccharide **conjugate**
IT Anti-inflammatory agents
Antitumor agents
Drug bioavailability
(anticancer and antiinflammatory drug-polysaccharide **conjugates**)
IT Polysaccharides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**conjugates** with anticancer and antiinflammatory drugs and peptide spacers; anticancer and antiinflammatory drug-polysaccharide **conjugates**)

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**conjugates** with anticancer and antiinflammatory drugs and polysaccharides; anticancer and antiinflammatory drug-polysaccharide **conjugates**)

IT 56-40-6DP, Glycine, **conjugates** with antitumor and antiinflammatory drugs and polysaccharides, biological studies 637-84-3DP, **conjugates** with antitumor and antiinflammatory drugs and polysaccharides 721-90-4DP, **conjugates** with antitumor and antiinflammatory drugs and polysaccharides 9004-54-0DP, Dextran, oxidation and reduction derivs., **conjugates** with antitumor and antiinflammatory drugs and peptide spacers, biological studies 14656-09-8DP, **conjugates** with antitumor and antiinflammatory drugs and polysaccharides 23214-92-8DP, Doxorubicin, **conjugates** with peptide spacers and polysaccharides 66328-74-3DP, **conjugates** with antitumor and antiinflammatory drugs and polysaccharides 143655-66-7DP, **conjugates** with peptide spacers and polysaccharides 171335-80-1DP, **conjugates** with peptide spacers and polysaccharides 184585-36-2DP, **conjugates** with antitumor and antiinflammatory drugs and polysaccharides **200427-88-9DP**, **conjugates** with antitumor and antiinflammatory drugs and polysaccharides 200427-89-0DP, **conjugates** with antitumor and antiinflammatory drugs and polysaccharides 200428-32-6DP, **conjugates** with peptide spacers and polysaccharides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(anticancer and antiinflammatory drug-polysaccharide **conjugates**)

L4 ANSWER 22 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:1392 CAPLUS
DOCUMENT NUMBER: 128:66509
TITLE: Drug complexes
INVENTOR(S): Inoue, Kazuhiro; Susaki, Hiroshi; Ikeda, Masahiro; Kuga, Hiroshi; Kumazawa, Eiji; Togo, Akiko
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan; Drug Delivery System Institute, Ltd.; Inoue, Kazuhiro; Susaki, Hiroshi; Ikeda, Masahiro; Kuga, Hiroshi; Kumazawa, Eiji; Togo, Akiko
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9746260	A1	19971211	WO 1997-JP1914	19970605

W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

TW 527183	B	20030411	TW 1997-86107455	19970531
AU 9729787	A1	19980105	AU 1997-29787	19970605
AU 723392	B2	20000824		
EP 916348	A1	19990519	EP 1997-924325	19970605
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
CN 1227499	A	19990901	CN 1997-197008	19970605
NO 9805666	A	19990204	NO 1998-5666	19981204
KR 2000016558	A	20000325	KR 1998-710148	19981207
US 6436912	B1	20020820	US 1999-147342	19990325
US 2003171262	A1	20030911	US 2002-155170	20020528

PRIORITY APPLN. INFO.: JP 1996-144421 A 19960606
WO 1997-JP1914 W 19970605
US 1999-147342 A3 19990325

AB The invention relates to drug complexes wherein a carboxy (C1-4)alkyldextran polyalc., which has been treated under such conditions as to allow the substantially complete formation of the polyalc., is bonded to the residue of a medicinal compound such as an antitumor agent [e.g. doxorubicin] via a spacer consisting of one amino acid or a spacer consisting of two to eight amino acids bonded to each other via peptide bonds. The complexes are excellent in the tumor site selectivity and thus can exhibit a high antitumor effect with relieved expression of toxicity.

IC ICM A61K047-48

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

ST antitumor drug dextran polyalc **conjugate**; antiinflammatory drug dextran polyalc **conjugate**; bioavailability drug dextran polyalc **conjugate**

IT Anti-inflammatory agents
Antitumor agents
Drug bioavailability
(antitumor or antiinflammatory drug dextran polyalc. **conjugates**)

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**conjugates** with antitumor or antiinflammatory drugs and carboxyalkyldextran polyalcs.; antitumor or antiinflammatory drug dextran polyalc. **conjugates**)

IT 637-84-3D, **conjugates** with antitumor or antiinflammatory drugs and carboxyalkyldextran polyalcs. 23214-92-8D, Doxorubicin, **conjugates** with peptide spacer and carboxyalkyldextran polyalcs. 143655-66-7D, DW 8089, **conjugates** with peptide spacers and carboxyalkyldextran polyalcs. 171335-80-1D, **conjugates** with peptide spacer and carboxyalkyldextran polyalcs. 184585-36-2D, D 51-7059, **conjugates** with peptide spacers and carboxyalkyldextran polyalcs. **200427-88-9D**, **conjugates** with antitumor or antiinflammatory drugs and carboxyalkyldextran polyalcs. 200438-24-0D, DW 8286, **conjugates** with peptide spacers and carboxyalkyldextran polyalcs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor or antiinflammatory drug dextran polyalc. **conjugates**)

IT 56-40-6DP, Glycine, **conjugates** with antitumor or antiinflammatory drugs and carboxyalkyldextran polyalcs., preparation 721-90-4DP, **conjugates** with antitumor or antiinflammatory drugs and carboxyalkyldextran polyalcs. 9004-54-0DP, Dextran, oxidation and reduction

derivs., **conjugates** with peptide spacers and antitumor or antiinflammatory drugs and carboxyalkyldextran polyalcs., preparation 14656-09-8DP, **conjugates** with antitumor or antiinflammatory drugs and carboxyalkyldextran polyalcs. 66328-74-3P 200427-89-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(antitumor or antiinflammatory drug dextran polyalc. **conjugates**
)

L4 ANSWER 23 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:706907 CAPLUS
DOCUMENT NUMBER: 128:30115
TITLE: Antitumor effects and toxicities of carboxymethylpullulan-peptide-doxorubicin **conjugates**
AUTHOR(S): Nogusa, Hideo; Yano, Toshiro; Kajiki, Masahiro; Gonsho, Akinori; Hamana, Hiroshi; Okuno, Satoshi
CORPORATE SOURCE: Drug Delivery System Institute, Ltd., Noda, 278, Japan
SOURCE: Biological & Pharmaceutical Bulletin (1997), 20(10), 1061-1065
CODEN: BPBLEO; ISSN: 0918-6158
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In vivo antitumor effects of the conjugates of doxorubicin (DXR) with carboxymethylpullulan (CMPul) through tetrapeptide spacers were compared with those of DXR against tumor-bearing rats. CMPul-DXR conjugates bound through Gly-Gly-Phe-Gly and Gly-Phe-Gly-Gly spacers were found to be more potent than DXR after a single i.v. injection in rats bearing Walker 256 carcinosarcoma. These conjugates were also more effective than DXR in rats bearing Yoshida sarcoma. However, CMPul-DXR conjugate bound through Gly-Gly-Gly-Gly was less effective against Walker 256-bearing rats than DXR. Body weight loss of CMPul-DXR conjugates in rats, on the other hand, was less than that of DXR at a DXR dose of 10 mg/kg. LDs of CMPul-DXR conjugates in CDF1 mice were about 3-times higher than that of DXR. These data suggest that the therapeutic index of CMPul-DXR conjugates bound through appropriate peptide spacers was increased more than that of DXR. However, CMPul-DXR conjugates tested were all less effective than DXR against Walker 256 cells in vitro. Also, 125I-labeled CMPul-DXR conjugate accumulated much less in the cells than 14C-DXR.
CC 1-6 (Pharmacology)
ST antitumor carboxymethylpullulan peptide doxorubicin **conjugate**
IT Antitumor agents
(antitumor effects and toxicities of carboxymethylpullulan-peptide-doxorubicin **conjugates**)
IT **161254-06-4** 161254-07-5 161254-12-2
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor effects and toxicities of carboxymethylpullulan-peptide-doxorubicin **conjugates**)
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:211123 CAPLUS
DOCUMENT NUMBER: 126:199707
TITLE: Camptothecin derivatives
INVENTOR(S): Tsujihara, Kenji; Kawaguchi, Takayuki; Okuno, Satoshi; Yano, Toshiro

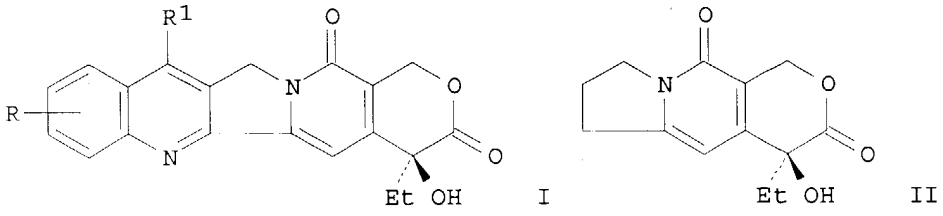
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 53 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 757049	A1	19970205	EP 1996-305579	19960730
EP 757049	B1	19990324		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AU 9660698	A1	19970206	AU 1996-60698	19960725
AU 717653	B2	20000330		
ZA 9606323	A	19970227	ZA 1996-6323	19960725
IL 118957	A1	20001121	IL 1996-118957	19960725
IL 127135	A1	20001206	IL 1996-127135	19960725
IL 131372	A1	20010319	IL 1996-131372	19960725
CA 2182244	AA	19970203	CA 1996-2182244	19960729
CA 2182244	C	20040203		
JP 10072467	A2	19980317	JP 1996-198939	19960729
JP 3332735	B2	20021007		
US 5837673	A	19981117	US 1996-689018	19960730
AT 178067	E	19990415	AT 1996-305579	19960730
ES 2131913	T3	19990801	ES 1996-305579	19960730
BG 63342	B1	20011031	BG 1996-100758	19960731
NO 9603214	A	19970203	NO 1996-3214	19960801
BR 9603253	A	19980428	BR 1996-3253	19960801
RU 2138503	C1	19990927	RU 1996-115394	19960801
CN 1145365	A	19970319	CN 1996-106979	19960802
CN 1075501	B	20011128		
TW 466242	B	20011201	TW 1996-85109331	19960802
HK 1005545	A1	20000414	HK 1998-104671	19980529
CN 1308078	A	20010815	CN 2000-132661	20001122

PRIORITY APPLN. INFO.: JP 1995-197391 A 19950802
JP 1995-340619 A 19951227
JP 1996-173372 A 19960703
IL 1996-118957 A3 19960725
IL 1996-127135 A3 19960725

OTHER SOURCE(S): MARPAT 126:199707

GI



AB Camptothecin derivs. I [R = aminoalkoxy, optionally bound to a polysaccharide having carboxyl groups via an amino acid or peptide; R1 = (un)substituted alkyl] were prepared I show enhanced antitumor activities but few side effects (no data). Thus, 10-(3-aminopropoxy)-7-ethyl-(20S)-

camptothecin.HCl was prepared from H2N(CH2)3OH, 5,2-HO(O2N)C6H3CHO, and the pyranoindole II in 8 steps and was converted to its glycyl-glycyl-L-phenylalanyl-glycylaminopropoxy derivative which was treated with carboxymethyldextran Na salt to give the conjugate.

IC ICM C07D491-22
ICS A61K047-48; C08B037-00; C07K007-00; C07K005-00

CC 31-5 (Alkaloids)
Section cross-reference(s): 1

ST dextran **conjugate** peptidylaminoalkoxycamptothecin prepn antitumor; camptothecin peptidylaminoalkoxy dextran **conjugate** prepn antitumor

IT Antitumor agents
(preparation of dextran **conjugates** of peptidylaminoalkoxy(ethyl)camptothecin)

IT 156-87-6, 3-Aminopropanol 3262-72-4, N-tert-Butoxycarbonyl-L-serine 3978-80-1, N-tert-Butoxycarbonyl-L-tyrosine 9004-54-0, Dextran, reactions 9057-02-7, Pullulan 15761-38-3, N-tert-Butoxycarbonyl-L-alanine 17302-47-5 25616-33-5 42454-06-8, 5-Hydroxy-2-nitrobenzaldehyde 110351-94-5 174308-47-5 **187794-49-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of dextran **conjugates** of peptidylaminoalkoxy(ethyl)camptothecin)

IT 39422-83-8P, Carboxymethyldextran sodium salt 58885-58-8P 80909-96-2P 109116-58-7P, Pullulan, carboxymethyl ether, sodium salt 187793-42-6P 187793-43-7P 187793-44-8P 187793-45-9P 187793-46-0P 187793-48-2P 187793-50-6P 187793-52-8P 187793-54-0P 187793-56-2P 187793-62-0P 187793-67-5P 187793-69-7P 187793-74-4P 187793-76-6P **187793-78-8P 187793-80-2P 187793-84-6P** **187793-86-8P** 187793-88-0P 187793-90-4P 187794-01-0P 187794-03-2P 187794-05-4P 187794-07-6P 187794-11-2P 187794-17-8P 187794-19-0P 187794-20-3P 187794-22-5P 187794-23-6P 187794-25-8P 187794-26-9P 187794-28-1P 187794-29-2P 187794-31-6P 187794-32-7P 187794-34-9P 187794-35-0P 187794-37-2P 187794-38-3P 187794-40-7P 187794-41-8P 187794-43-0P 187794-44-1P 187794-46-3P 187794-47-4P **187794-48-5P 187794-50-9P 187794-53-2P** **187794-55-4P 187794-60-1P** 187794-66-7P 187794-68-9P 187794-72-5P **187794-74-7P** 187803-36-7P 187803-37-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of dextran **conjugates** of peptidylaminoalkoxy(ethyl)camptothecin)

IT 187793-58-4P 187793-60-8P 187793-65-3P 187793-71-1P 187794-09-8P 187794-13-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of dextran **conjugates** of peptidylaminoalkoxy(ethyl)camptothecin)

IT **187793-82-4P** 187794-21-4P 187794-24-7P 187794-27-0P 187794-30-5P 187794-33-8P 187794-36-1P 187794-39-4P 187794-42-9P 187794-45-2P 187794-58-7P 187794-70-3P **187852-47-7P** 187852-48-8P **187852-49-9P 187852-50-2P** 187852-51-3P 187852-52-4P 187852-53-5P 187852-54-6P **187852-55-7P** **187852-56-8P** 187852-57-9P **187852-58-0P** **187852-59-1P** 187852-60-4P 187852-61-5P **187852-62-6P** 187852-63-7P 187852-64-8P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of dextran **conjugates** of peptidylaminoalkoxy(ethyl)camptothecin)

L4 ANSWER 25 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:494751 CAPLUS
DOCUMENT NUMBER: 125:204516
TITLE: Diagnostic and therapeutic pretargeting methods using metal chelates
INVENTOR(S): Yau, Eric K.; Theodore, Louis J.; Gustavson, Linda M.
PATENT ASSIGNEE(S): Neorx Corporation, USA
SOURCE: U.S., 68 pp., Cont.-in-part of U.S. Ser. No. 156,565,abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5541287	A	19960730	US 1994-345811	19941122
US 5283342	A	19940201	US 1992-895588	19920609
EP 1138334	A2	20011004	EP 2001-201994	19930607
EP 1138334	A3	20020403		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
US 6022966	A	20000208	US 1993-156565	19931122
US 5911969	A	19990615	US 1994-329617	19941026
US 5847121	A	19981208	US 1995-571816	19951213

PRIORITY APPLN. INFO.:

US 1992-895588	A2	19920609
US 1992-995381	B2	19921223
US 1993-156565	B2	19931122
US 1992-995383	A	19921223
EP 1993-915235	A3	19930607
WO 1993-US5406	A2	19930607
US 1994-345811	A3	19941122

OTHER SOURCE(S): CASREACT 125:204516; MARPAT 125:204516

AB Methods, compds., compns., and kits that relate to pretargeted delivery of diagnostic (e.g. imaging) and therapeutic agents are disclosed. A targeting moiety-antiligand conjugate is administered in vivo; upon target localization of this conjugate (pretargeting) and clearance of the conjugate from the circulation, an active agent-ligand conjugate is parenterally administered,. Alternatively, a targeting moiety-ligand conjugate is administered in vivo; upon target localization and clearance of the conjugate from the circulation, an active agent-antiligand conjugate is parenterally administered. A preferred ligand-antiligand pair is biotin and avidin. Preferred targeting moieties are antibodies, antibody fragments, peptides, hormones, oligonucleotides, and cell surface receptor proteins. Preferred active agents are toxins, antitumor agents, drugs, and radionuclides. In particular, methods for production of low-mol.-weight radioiodinated biotin derivs., and for radiometal labeling of biotin and related compds. with 99mTc, 186Re, and 188Re by conjugation with a metal-chelating moiety are described. Thus, p-aminobenzyl-1,4,7,10-tetraazacyclododecane-N,N',N",N'"-tetraacetic acid (I) was prepared in several steps from N-tert-butoxycarbonylglycine p-nitrophenyl ester, ethylenediamine, and N-iodoacetyl-p-nitrophenylalanine using benzotriazolyloxytris(dimethylamino)phosphonium hexafluorophosphate for cyclocondensation; I was then coupled with N-biotinyl-N-methylglycine and complexed with 90Y. The chelate and its sulfoxide radiolysis product bound to avidin.

IC ICM A61K038-12
ICS C07K005-00
NCL 530317000
CC 63-6 (Pharmaceuticals)
ST antitumor pretargeting biotin **conjugate** avidin; radioelement

biotin chelate targeting tumor; imaging radioelement chelate **conjugate** targeting

IT Neoplasm
(imaging of, with radioelement chelate-biotin **conjugates**; diagnostic and therapeutic pretargeting methods using metal chelates)

IT Neoplasm inhibitors
(radioelement chelate-biotin **conjugates**; diagnostic and therapeutic pretargeting methods using metal chelates)

IT Albumins, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biotinylated, galactosylated, antibody-streptavidin **conjugate** clearance from blood in response to; diagnostic and therapeutic pretargeting methods using metal chelates)

IT Avidins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**conjugates**, complexation with biotinylated antibody, for pretargeting; diagnostic and therapeutic pretargeting methods using metal chelates)

IT Biological transport
(endocytosis, of radiolabeled biotin **conjugate**, pretargeting in relation to; diagnostic and therapeutic pretargeting methods using metal chelates)

IT 58-85-5DP, D-Biotin, **conjugates** with radioactive metal chelates
9004-54-0DP, Dextran, biotinylated, radiolabeled 180737-57-9P
180737-58-0P 180737-59-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(diagnostic and therapeutic pretargeting methods using metal chelates)

IT 25104-18-1D, Polylysine, **conjugates** with biotin and chelating agents 38000-06-5D, Polylysine, **conjugates** with biotin and chelating agents
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostic and therapeutic pretargeting methods using metal chelates)

IT 1926-80-3P, Methyl 6-aminocaproate hydrochloride 3655-05-8P
14273-90-6P, Methyl 6-bromocaproate 33305-77-0P 41236-09-3P
53871-85-5P 81393-85-3P 116052-88-1P 116052-89-2P 116052-94-9P
116366-32-6P 143841-34-3P 154024-64-3P 154024-65-4P 154024-67-6P
154024-68-7P 154024-69-8P 154024-72-3P, Biotinyl-D-alanine
154024-74-5P 154024-75-6P 154024-76-7P 167861-55-4P 167861-58-7P
167861-59-8P 167861-60-1P **167861-61-2P** **167861-62-3P**
167861-73-6P **167861-74-7P** 180737-49-9P **180737-51-3P**
180737-52-4P 180737-53-5P 180737-54-6P **180737-55-7P**
180737-56-8P 180978-51-2P 180978-52-3P 180978-53-4P
180978-54-5P 181065-46-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(diagnostic and therapeutic pretargeting methods using metal chelates)

IT 64987-85-5D, SMCC, **conjugates** with avidin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(radiolabeled biotin **conjugate** pretargeting with; diagnostic and therapeutic pretargeting methods using metal chelates)

IT 154024-49-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tumor cell targeting with avidin **conjugate** and; diagnostic and therapeutic pretargeting methods using metal chelates)

L4 ANSWER 26 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:158255 CAPLUS
DOCUMENT NUMBER: 124:317848
TITLE: Benzenesulfonamide-peptide **conjugates** as probes for secondary binding sites near the active site of carbonic anhydrase
AUTHOR(S): Sigal, George B.; Whitesides, George M.
CORPORATE SOURCE: Dep. Chem., Harvard Univ., Cambridge, MA, 02138, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1996), 6(5), 559-64
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Libraries of N-(4-sulfamoylbenzoyl)oligoglycines terminated with different L-amino acids were screened to identify tight binding inhibitors of human carbonic anhydrase II. Inhibitors terminated with hydrophobic amino acids showed significant enhancements in binding compared to the corresponding glycine derivs. No enhancements were observed due to polar interactions.

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 7

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(benzenesulfonamide **conjugate**; preparation and carbonic anhydrase active side binding of benzenesulfonamide-peptide **conjugates**)

IT Combinatorial library
(peptide; preparation and carbonic anhydrase active side binding of benzenesulfonamide-peptide **conjugates**)

IT Molecular structure-biological activity relationship
(carbonate dehydratase-binding, preparation and carbonic anhydrase active side binding of benzenesulfonamide-peptide **conjugates**)

IT 9001-03-0, Carbonic anhydrase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(human II; preparation and carbonic anhydrase active side binding of benzenesulfonamide-peptide **conjugates**)

IT 143288-21-5 165682-39-3 165682-40-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(preparation and carbonic anhydrase active side binding of benzenesulfonamide-peptide **conjugates**)

IT **165682-42-8P** 165682-43-9P 176170-35-7P 176170-36-8P
176170-37-9P 176170-38-0P 176170-39-1P 176170-40-4P 176170-41-5P
176170-42-6P 176170-43-7P 176170-44-8P 176170-45-9P 176170-46-0P
176170-47-1P 176170-48-2P 176170-49-3P 176170-50-6P 176170-51-7P
176170-52-8P 176170-53-9P 176170-54-0P 176170-55-1P 176170-56-2P
176170-57-3P 176170-58-4P 176170-59-5P 176170-60-8P 176170-61-9P
176170-62-0P 176170-63-1P 176170-64-2P 176170-65-3P 176170-66-4P
176170-67-5P 176170-68-6P 176170-69-7P 176170-70-0P 176170-71-1P
176170-72-2P 176170-73-3P 176170-74-4P 176170-75-5P 176170-76-6P
176170-77-7P 176170-78-8P 176170-79-9P 176170-80-2P 176170-81-3P
176170-82-4P 176170-83-5P 176170-84-6P 176170-85-7P 176170-86-8P
176170-87-9P 176170-88-0P 176170-89-1P 176170-90-4P 176170-91-5P
176170-92-6P 176170-93-7P 176170-94-8P 176170-95-9P 176170-96-0P
176170-97-1P 176170-98-2P 176170-99-3P 176171-00-9P 176171-01-0P
176171-02-1P 176171-03-2P 176171-04-3P 176171-05-4P 176171-06-5P

176171-07-6P 176171-08-7P 176171-09-8P 176171-10-1P
176171-11-2P 176171-12-3P 176171-13-4P 176171-14-5P 176171-15-6P
176171-16-7P **176171-17-8P 176171-18-9P**
176171-19-0P 176171-20-3P 176171-21-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and carbonic anhydrase active side binding of benzenesulfonamide-peptide **conjugates**)

IT 56-40-6, Glycine, reactions 56-41-7, L-Alanine, reactions 56-45-1, Serine, reactions 56-84-8, Aspartic acid, reactions 56-85-9, Glutamine, reactions 56-86-0, Glutamic acid, reactions 61-90-5, Leucine, reactions 63-68-3, Methionine, reactions 63-91-2, L-Phenylalanine, reactions 70-47-3, Asparagine, reactions 72-18-4, Valine, reactions 72-19-5, Threonine, reactions 73-32-5, Isoleucine, reactions 74-79-3, L-Arginine, reactions 138-41-0 147-85-3, Proline, reactions 327-57-1, Norleucine 943-80-6, p-Amino-L-phenylalanine 949-99-5, p-Nitro-L-phenylalanine 1132-68-9, p-Fluoro-L-phenylalanine 6230-11-1, O-Methyltyrosine 14173-39-8, p-Chloro-L-phenylalanine 20859-02-3, L-tert-Leucine 58438-03-2, 3-(2-Naphthyl)-L-alanine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and carbonic anhydrase active side binding of benzenesulfonamide-peptide **conjugates**)

IT 67460-24-6P 154715-61-4P 176170-33-5P 176170-34-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and carbonic anhydrase active side binding of benzenesulfonamide-peptide **conjugates**)

L4 ANSWER 27 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:966994 CAPLUS
DOCUMENT NUMBER: 124:176877
TITLE: Synthesis of carboxymethylpullulan-peptide-doxorubicin **conjugates** and their properties
AUTHOR(S): Nogusa, Hideo; Yano, Toshiro; Okuno, Satoshi; Hamana, Hiroshi; Inoue, Kazuhiro
CORPORATE SOURCE: Drug Delivery System Inst., Ltd., Chiba, 278, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1995), 43(11), 1931-6
CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The amino group of doxorubicin (DXR) was found to be bound to the carboxyl group of carboxymethylpullulan (CMPul) either directly or through tetrapeptide spacers, including Gly-Gly-Phe-Gly, Gly-Phe-Gly-Gly and Gly-Gly-Gly-Gly. These conjugates had DXR contents of 6.1-7.1%, with the degree of substitution of carboxymethyl groups being 0.6 per sugar moiety. These conjugates associate in phosphate-buffered saline (PBS) (pH 7.4), forming micelles with hydrophobic DXR inside and hydrophilic CMPul on the outside. The amts. of DXR released from the conjugates in the presence of rat liver lysosomal enzymes were determined by HPLC. The rate of drug release differed among the conjugates tested. CMPul-DXR conjugate bound through Gly-Gly-Phe-Gly released 35% of its DXR over 24 h. On the other hand, CMPul-DXR conjugate without spacer released no free DXR. The antitumor effect of each conjugate in rats bearing Walker 256 was studied by monitoring the tumor wts. after a single i.v. injection. Compared with DXR, CMPul-DXR conjugates bound through Gly-Gly-Phe-Gly and Gly-Phe-Gly-Gly spacers significantly suppressed the tumor growth, while CMPul-DXR conjugate bound through Gly-Gly-Gly-Gly showed less antitumor

effect than DXR. CMPul-DXR conjugate without spacer showed no in vivo antitumor effect even at a dose equivalent to as much as 20 mg/kg of DXR.

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 33

ST peptide carboxymethylpullulan doxorubicin **conjugate** prepn antitumor; pullulan carboxymethyl **conjugate** prepn antitumor

IT Neoplasm inhibitors
(synthesis of carboxymethylpullulan-peptide-doxorubicin **conjugates** and their antitumor activities)

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(**conjugates**, synthesis of carboxymethylpullulan-peptide-doxorubicin **conjugates** and their antitumor activities)

IT Molecular structure-biological activity relationship
(neoplasm-inhibiting, synthesis of carboxymethylpullulan-peptide-doxorubicin **conjugates** and their antitumor activities)

IT 23214-92-8DP, Doxorubicin, reaction products with sodium carboxymethylpullulan **161254-06-4DP**, reaction products with sodium carboxymethylpullulan 161254-07-5DP, reaction products with sodium carboxymethylpullulan 161254-12-2DP, reaction products with sodium carboxymethylpullulan
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of carboxymethylpullulan-peptide-doxorubicin **conjugates** and their antitumor activities)

IT 79-11-8, reactions 556-50-3, Glycylglycine 721-90-4, Phenylalanylglycine 1738-82-5 3321-03-7, Glycylphenylalanine 9057-02-7, Pullulan 23214-92-8, Doxorubicin
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of carboxymethylpullulan-peptide-doxorubicin **conjugates** and their antitumor activities)

IT 79-11-8DP, reaction products with pullulan 5893-07-2P 9057-02-7DP, Pullulan, reaction products with chloroacetic acid, sodium salt 17293-97-9P 76378-71-7P **161254-06-4P** 161254-07-5P 161254-12-2P **173723-56-3P** 173723-57-4P **173723-58-5P** 173723-59-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of carboxymethylpullulan-peptide-doxorubicin **conjugates** and their antitumor activities)

IT 104095-57-0P 161254-11-1P **161254-16-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of carboxymethylpullulan-peptide-doxorubicin **conjugates** and their antitumor activities)

L4 ANSWER 28 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:795164 CAPLUS
DOCUMENT NUMBER: 123:225940
TITLE: Pretargeting methods and compounds comprising radiometal labeled biotin and biotin- or streptavidin-antibody **conjugates**
INVENTOR(S): Yau, Eric K.; Theodore, Louis J.; Gustavson, Linda M.
PATENT ASSIGNEE(S): Neorx Corp., USA
SOURCE: PCT Int. Appl., 180 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9515335	A2	19950608	WO 1994-US13485	19941122
WO 9515335	A3	19950720		
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6022966	A	20000208	US 1993-156565	19931122
EP 736035	A1	19961009	EP 1995-910066	19941122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09505831	T2	19970610	JP 1995-515670	19941122

PRIORITY APPLN. INFO.:
US 1993-156565 A 19931122
US 1992-895588 A2 19920609
US 1992-995381 B2 19921223
WO 1993-US5406 A2 19930607
WO 1994-US13485 W 19941122

AB Methods, compds., compns. and kits that relate to pretargeted delivery of diagnostic and therapeutic agents are disclosed. In particular, methods for radiometal labeling of biotin, as well as related compds., are described. Articles of manufacture useful in pretargeting methods are also discussed. In example, 186Re-chelated biotin and biotinylated monoclonal antibody to human colon tumor (NR-LU-10) were prepared and used in combination with avidin were performed in a 3-step pretargeting protocol in nude mice implanted with human colon tumor xenografts, and a enhanced tumor uptake of 186Re-chelated biotin in the presence of biotinylated antibody and avidin was observed Also, streptavidin-NR-LU-10 conjugates were prepared and used in combination with 186Re-chelated biotin and asialoorosomucoid clearing agent (preparation described) for two-step pretargeting protocol experiment

IC ICM C07K001-08
CC 15-3 (Immunochemistry)
Section cross-reference(s): 8, 34, 63
ST radiometal biotin **conjugate** biotinylated antibody; streptavidin monoclonal antibody **conjugate** tumor targeting
IT Orosomucoids
RL: MOA (Modifier or additive use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(asialo-; **conjugates**; radiometal-labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)
IT Radioelements, biological studies
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(metal; chelate; **conjugates**; radiometal-labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)
IT Neoplasm
(pretargeting; radiometal-labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)
IT Metals, biological studies
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(radio-; chelate; **conjugates**; radiometal-labeled biotin and **conjugates** of antibody and biotin or streptavidin in

pretargeting method for tumor diagnosis and therapy)

IT Neoplasm inhibitors
(radiometal-labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)

IT Intestine, neoplasm
(colon, radiometal labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)

IT Albumins, biological studies
RL: MOA (Modifier or additive use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**conjugates**, radiometal labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)

IT Antibodies
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(**conjugates**, radiometal labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)

IT Avidins
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(**conjugates**, radiometal labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)

IT Antibodies
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(monoclonal, **conjugates**; radiometal labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)

IT Peptides, reactions
RL: MOA (Modifier or additive use); RCT (Reactant); RACT (Reactant or reagent); USES (Uses)
(tetra-, acyclic; radiometal-labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)

IT Amides, reactions
RL: MOA (Modifier or additive use); RCT (Reactant); RACT (Reactant or reagent); USES (Uses)
(tetra-, cyclic; radiometal labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)

IT Peptides, reactions
RL: MOA (Modifier or additive use); RCT (Reactant); RACT (Reactant or reagent); USES (Uses)
(tri-, acyclic; radiometal-labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)

IT 59-23-4D, Galactose, albumin **conjugates** 9004-54-0, Dextran, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as clearing agent; radiometal-labeled biotin and **conjugates**

of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)

IT 9013-20-1P, Streptavidin
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(**conjugates**; radiometal-labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)

IT 56602-33-6
RL: MOA (Modifier or additive use); USES (Uses)
(radiometal-labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)

IT 60-32-2, 6-Aminocaproic acid 107-97-1, N-Methylglycine 949-99-5 2389-60-8 3655-05-8 4224-70-8, 6-Bromocaproic acid 31954-27-5 167861-71-4 167861-72-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(radiometal-labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)

IT 556-33-2P, Triglycine 2780-89-4P, Methyl 6-aminocaproate 14273-90-6P, Methyl 6-bromocaproate 28320-73-2P 33305-77-0P 35013-72-0P 41236-09-3P 53871-85-5P 53906-36-8P 62222-21-3P 69705-14-2P 81393-85-3P 87548-77-4P 116052-89-2P 116366-32-6P 123317-52-2P 135825-00-2P 143841-34-3P 154024-43-8P 154024-45-0P 154024-64-3P 154024-65-4P 154024-67-6P 154024-68-7P 154024-75-6P 154024-76-7P 167861-56-5P 167861-58-7P 167861-59-8P 167861-60-1P **167861-61-2P 167861-62-3P 167861-63-4P** **167861-64-5P** 167861-65-6P 167861-66-7P 167861-68-9P 167861-69-0P 167861-73-6P **167861-74-7P** 167861-75-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(radiometal-labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)

IT 154024-42-7P 167861-67-8P 167861-70-3P 167861-76-9P
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(radiometal-labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)

IT 14133-76-7DP, Technetium-99, complexes with chelate-biotin **conjugate**, biological studies 14998-63-1DP, Rhenium-186, complexes with chelate-biotin **conjugate**, biological studies 60239-18-1DP, 1,4,7,10-Tetraazacyclododecane-N,N',N'', N'''-tetraacetic acid, derivs.; complexes; **conjugates** 123317-51-1DP, complexes; **conjugates** 154024-46-1DP, rhenium-186 and technetium-99 complexes 154024-46-1P 167861-53-2DP, rhenium-186 and technetium-99 complexes 167861-53-2P 167861-54-3DP, rhenium-186 and technetium-99 complexes 167861-54-3P 167861-55-4DP, rhenium-186 and technetium-99 complexes 167861-55-4P 167861-57-6DP, iodine labeled
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(radiometal-labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)

L4 ANSWER 29 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1995:386032 CAPLUS
DOCUMENT NUMBER: 122:299074
TITLE: Polysaccharide derivative and drug **carrier**
INVENTOR(S): Nogusa, Hideo; Hamana, Hiroshi; Yano, Toshiro; Kajiki, Masahiro; Yamamoto, Keiji; Okuno, Satoshi; Sugawara, Shuichi; Kashima, Nobukazu; Inoue, Kazuhiro
PATENT ASSIGNEE(S): Drug Delivery System Institute, Ltd., Japan
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9419376	A1	19940901	WO 1994-JP322	19940228
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2134348	AA	19940827	CA 1994-2134348	19940228
EP 640622	A1	19950301	EP 1994-907702	19940228
EP 640622	B1	20000809		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AT 195324	E	20000815	AT 1994-907702	19940228
ES 2149867	T3	20001116	ES 1994-907702	19940228
PT 640622	T	20001130	PT 1994-94907702	19940228
US 5688931	A	19971118	US 1994-325296	19941228
GR 3034416	T3	20001229	GR 2000-402104	20000918

PRIORITY APPLN. INFO.: JP 1993-38635 A 19930226
WO 1994-JP322 W 19940228

AB A novel polysaccharide derivative [e.g. sodium carboxymethyl pullulan-3'-N-(Gly-Gly-Phe-Gly)-doxorubicin] is prepared and a drug carrier and a drug composite both comprise said derivative The derivative is a carboxylated polysaccharide wherein a peptide chain composed of one to 8 same or different amino acids is introduced into part or all of the carboxyl groups of the polysaccharide and wherein part or all of those amino or carboxyl groups of the peptide chain which do not participate in the above linkage to the carboxyl groups of the polysaccharide may be bonded to the carboxyl, amino or hydroxyl groups of another compound (e.g. a drug) through amide or ester bonds. The derivative can migrate to the tumor-bearing region so readily that it can efficiently send drugs which are problematic in the side effects or have limited persistence of the drug activity in the tumor-bearing region.

IC ICM C08B037-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
ST polysaccharide deriv prepn drug **carrier**
IT Neoplasm inhibitors
Pharmaceutical dosage forms
(preparation of polysaccharide derivative as drug **carrier**)
IT Polysaccharides, biological studies
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of polysaccharide derivative as drug **carrier**)
IT 5893-05-0 9057-02-7, Pullulan 9064-52-2 9067-32-7, Hyaluronic acid sodium salt 23214-92-8D, Doxorubicin, derivs. 39422-83-8, Sodium carboxymethyl dextran 64859-64-9 76378-71-7 104095-57-0 105156-94-3 161254-03-1 161254-04-2 **161254-06-4** 161254-08-6 161254-11-1 161254-13-3 161254-15-5 **161254-16-6** 163254-82-8

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of polysaccharide derivative as drug **carrier**)

IT 109116-58-7DP, reaction products with doxorubicin derivs. 109116-58-7P 161254-05-3P 161254-07-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of polysaccharide derivative as drug **carrier**)

IT 23214-92-8, Doxorubicin
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(preparation of polysaccharide derivative as drug **carrier**)

IT 9064-52-2DP, reaction product with doxorubin derivs. 9067-32-7DP, reaction product with doxorubin derivs. 39422-83-8DP, Sodium carboxymethyldextran, reaction product with doxorubin derivs. 64859-64-9DP, reaction product with doxorubin derivs. 105156-94-3DP, reaction product with doxorubin derivs. 147513-69-7DP, reaction product with polysaccharides 147513-69-7P 161254-03-1DP, reaction product with polysaccharides 161254-05-3DP, reaction product with polysaccharides 161254-07-5DP, reaction product with polysaccharides 161254-09-7P 161254-10-0DP, reaction product with polysaccharides 161254-10-0P 161254-12-2DP, reaction product with polysaccharides 161254-12-2P 161254-14-4DP, reaction product with polysaccharides 161254-14-4P 163254-82-8DP, reaction product with doxorubin derivs.
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of polysaccharide derivative as drug **carrier**)

IT **161254-06-4DP**, reaction product with polysaccharides 161254-09-7DP, reaction product with polysaccharides
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of polysaccharide derivative as drug **carrier**)

L4 ANSWER 30 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:490207 CAPLUS
DOCUMENT NUMBER: 119:90207
TITLE: Synthesis, metal chelate stability studies, and enzyme digestion of a peptide-**linked** DOTA derivative and its corresponding radiolabeled immunoconjugates
AUTHOR(S): Li, Min; Meares, Claude F.
CORPORATE SOURCE: Dep. Chem., Univ. California, Davis, CA, 95616-0935, USA
SOURCE: Bioconjugate Chemistry (1993), 4(4), 275-83
CODEN: BCCHES; ISSN: 1043-1802
DOCUMENT TYPE: Journal
LANGUAGE: English

AB By directly coupling a tetrapeptide to DOTA through an amide bond, a novel DOTA derivative, DOTA-glycylglycylglycyl-L-p-nitrophenylalanine amide, was synthesized. This new precursor bifunctional chelating agent was converted to DOTA-glycylglycylglycyl-L-p-isothiocyanatophenylalanine and conjugated to monoclonal antibody Lym-1. Serum stability studies show that the radiolabeled conjugates are kinetically inert under physiol. conditions. The rates of loss of radiometals in human serum are 0.1% per day for In3+, 0.02% per day for Y3, and 0.3% per day for Cu2+-labeled immunoconjugates. In the presence of the liver enzyme cathepsin B, an in vitro digestion of 114mIn-labeled conjugate yields a small fragment containing 114mIn. Characterization of the cleavage products shows that this liver enzyme hydrolyzes the peptide linkage before the phenylalanine residue, freeing the In-DOTA-triglycine complex from the conjugate. However, the liver enzyme cathepsin D does not cleave the linkage over the span of 7 days.

CC 8-9 (Radiation Biochemistry)
IT Antibodies
RL: SPN (Synthetic preparation); PREP (Preparation)
(monoclonal, **conjugates**, with radiometals and peptide-**linked** DOTA derivative, preparation and stability and enzyme digestion of)
IT **149226-84-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and coupling with DOTA)
IT 13982-36-0DP, Yttrium-88, DOTA derivative-monoclonal antibody **conjugates** 15757-86-5P, Copper-67, preparation 149206-87-1DP, radiometal-monoclonal antibody **conjugates**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and stability and enzyme digestion of)
IT 13981-55-0DP, Indium-114, DOTA derivative-monoclonal antibody **conjugates**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and stability and enzyme digestion of metastable)
IT **149206-85-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and trifluoroacetylation of)
IT 9025-26-7, Cathepsin D 9047-22-7, Cathepsin B
RL: BIOL (Biological study)
(radiometal-DOTA derivative-monoclonal antibody **conjugate** digestion by)

L4 ANSWER 31 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1984:412062 CAPLUS
DOCUMENT NUMBER: 101:12062
TITLE: Enzymic cleavage of side chains of soluble polymers
AUTHOR(S): Labsky, Jiri; Mikes, Frantisek
CORPORATE SOURCE: VSCHT, Prague, Czech.
SOURCE: Sbornik Vysoke Skoly Chemicko-Technologicke v Praze, S: Polymery--Chemie, Vlastnosti a Zpracovani (1983), S 9, 279-308
CODEN: SVSZD5; ISSN: 0139-908X
DOCUMENT TYPE: Journal
LANGUAGE: Czech
AB Models were prepared for the study of release rates of biol. active substances (drugs, hormones, inhibitors, or enzymes) covalently bound to soluble organic polymers after endocytosis and exposure to liposomal hydrolases.
Soluble polymers, polymethacrylates or poly(hydroxypropylmethacrylamides) with d.p. 25-30, bound by amide bonds with L-phenylalanylnitroanilides through spacers of variable length and structure (peptides or aliphatic chains) were used as carriers. Chymotrypsin [9004-07-3]-catalyzed hydrolysis rates of the C-terminal anilide bonds were correlated with the length and structure of the spacers and the structure of the anilide groups. Steric conditions for the interactions of the spacer chains with chymotrypsin active site and affinity site are discussed.
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 7, 34
ST chymotrypsin hydrolysis polymethacrylate peptide anilide; drug **carrier** polymer
IT Pharmaceuticals
(**carriers** for, phenylalanylnitroanilide methacrylate polymers as models of)
IT 57950-58-0P 57950-81-9P 61435-96-9P 61435-97-0P **61435-98-1P**
61435-99-2P 61436-00-8P 62238-85-1P 64129-74-4P 64129-75-5P

64134-54-9P 64651-29-2P 70587-66-5P 70587-67-6P 70587-68-7P
71187-45-6P 73807-80-4P 73814-11-6P 90409-02-2P 90409-03-3P
90409-04-4P 90409-05-5P 90409-06-6P 90409-07-7P 90409-08-8P
90409-09-9P 90409-10-2P 90409-12-4P 90409-14-6P 90409-16-8P
90409-18-0P 90409-20-4P 90409-22-6P 90409-24-8P 90409-26-0P
90409-28-2P 90409-30-6P 90409-32-8P 90409-34-0P 90409-36-2P
90409-38-4P 90409-40-8P 90409-42-0P 90409-44-2P 90409-46-4P
90409-48-6P 90409-50-0P 90409-52-2P 90409-54-4P 90409-56-6P
90409-58-8P 90409-60-2P 90409-62-4P 90409-65-7P 90409-66-8P
90409-67-9P 90409-68-0P 90409-69-1P 90409-70-4P 90409-71-5P
90409-72-6P 90409-73-7P **90409-74-8P** 90409-76-0P
90426-73-6P 90426-75-8P 90426-77-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and chymotrypsin hydrolysis of, biomols. and drug release in relation to)

L4 ANSWER 32 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1980:501418 CAPLUS
DOCUMENT NUMBER: 93:101418
TITLE: Degradation of side chains of N-(2-hydroxypropyl)methacrylamide copolymers by lysosomal enzymes
AUTHOR(S): Duncan, Ruth; Lloyd, John B.; Kopecek, Jindrich
CORPORATE SOURCE: Dep. Biol. Sci., Univ. Keele, Keele/Staffordshire, ST5 5BG, UK
SOURCE: Biochemical and Biophysical Research Communications (1980), 94(1), 284-90
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of 22 N-(2-hydroxypropyl)methacrylamide copolymers, each containing a different, potential degradable side chain, were incubated with rat liver tritosomes. Four of the side chains were digestible as judged by the liberation of a terminal 4-nitroaniline residue. The pH optimum for the degradation of the side chain -ε-aminocaproyl-phenylalanyl-4-nitroanilide was in the range 5.75-6.5 over the first hour of incubation and somewhat lower (pH 5.5-6.0) after this time. The degradation of the above side chain had a Km value of 58.3 mg/mL. The use of these compds. as drug carrier mols. is discussed.
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 7, 34, 35
ST hydroxypropylmethacrylamide copolymer degrdn lysosome enzyme; drug **carrier** hydroxypropylmethylacrylamide copolymer; methacrylamide copolymer drug **carrier**
IT 53282-69-2DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 66493-40-1DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74541-62-1DP, reaction products with oligopeptides, nitrophenylamino containing 74569-67-8DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74569-69-0DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers **74569-71-4DP**, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74588-99-1DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-00-7DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-01-8DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-02-9DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-03-0DP,

reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-04-1DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-05-2DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-06-3DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-07-4DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-08-5DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-09-6DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-10-9DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-11-0DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-12-1DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-13-2DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-14-3DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-15-4DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and degradation of, by lysosomal enzymes, drug **carrier** in relation to)

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